UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Study Title: CC#15108 Pilot Randomized Pre-Surgical Evaluation of Agonist Anti-CD27 Monoclonal Antibody Varlilumab on Immunologic Activities of IMA950 Vaccine plus Poly-ICLC in Patients with WHO Grade II Low-Grade Glioma

This is a clinical trial, a type of research study. Your study doctors, Nicholas Butowski, MD, and Hideho Okada, MD, PhD, along with their colleagues at the UCSF Department of Neurosurgery will explain the clinical trial to you.

Clinical trials include only people who choose to take part. Please take your time reading the following information carefully and making your decision about participating. You may discuss your decision with your family, friends, and personal doctor (your primary care physician or general practitioner). If you have any questions, you may ask your study doctor.

You are being asked to take part in this investigational research study because you either have or are believed to have a type of brain tumor called a low-grade glioma for which you will undergo standard-of-care surgery.

Why is this study being done?

The purpose of this study is to find out what effects, good and/or bad, a vaccine has on your immune system and brain tumor. The hope is that the combination of these study drugs will be safe and reduce the likeliness that your tumor will recur.

The study drugs that will be evaluated in this study are a mixture of IMA950 and Poly-ICLC by injection given alone or in combination with Varlilumab by IV (infusion via a vein).

IMA950 is a study drug manufactured by Immatics, Inc., which may stimulate immune cells called T cells (a type of white blood cell) so they can identify and destroy cancer cells. IMA950 is considered experimental because it is not approved by the Food and Drug Administration (FDA).

Poly-ICLC (Polyinosinic-Polycytidylic acid with Poly-L-Lysine and Carboxymethylcellulose) is a study drug manufactured by Oncovir, Inc., which may enhance the immune response to the IMA950. Poly-ICLC has already been received and generally well tolerated by subjects in earlier studies and in some cases has been shown to decrease the size of brain tumors. Poly- ICLC is also considered experimental because it is not approved by the FDA.

Varlilumab (CDX-1127) is a study drug manufactured by Celldex Therapeutics, Inc., which may also enhance the immune response to the IMA950. Varlilumab may also bind to tumors cells directly and activate immune cell killing or stop the tumor cells from growing. Varlilumab is also considered experimental because it is not approved by the FDA.

Who pays for this study?

IMA950, Poly-ICLC, and Varlilumab are being provided free by Immatics, Inc., Oncovir, Inc., and Celldex Therapeutics, Inc., respectively. The research components of this study are being paid for by a grant from the National Cancer Institute (NCI).

Is there a potential conflict of interest for this study?

There are no known investigator and/or institutional conflicts of interest for this study.

How many people will take part in this study?

About 30 people will participate in this study at UCSF.

You cannot take part in the study if you are currently using any of the following treatments or medications:

- Radiation therapy
- Chemotherapy
- Interferon (e.g. Intron-A®)
- Allergy desensitization injections
- Growth factors (e.g., Procrit®, Aranesp®, Neulasta®)
- Interleukins (e.g., Proleukin®)
- Any investigational therapeutic medication

Study Location

All study procedures will be done at UCSF Medical Center. Some procedures considered routine may be done at local facilities and followed by the UCSF care team.

What will happen if I take part in this research study?

Before you begin the main part of the study...

SCREENING PROCEDURES

You will need to have the following exams, tests, or procedures to find out if you can be in the study. These exams, tests, or procedures are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

The following screening procedures will take about 2 hours total to complete and must be done within 28 days before registration to the study unless otherwise noted:

- Review of your **complete medical history** including any medications you are currently taking.
- **Physical and neurological examinations** including **vital signs** (pulse, breathing rate, blood pressure, and temperature), a measurement of your **height** and **weight**, and a **performance status** assessment (a measure of how well you are able to do your daily activities).

- **Brain MRI (Magnetic Resonance Imaging)** with and without contrast, which is a standard imaging procedure to look at the location and size of your tumor. The MRI will take about one hour to complete.
- **ECG** (also known as an **EKG** or **electrocardiogram**) is a test of the electrical and muscular functions of the heart and takes about 30 minutes to complete. It will be done for research purposes and would not be done if you were not taking part in the study.
- A **UCSF pathologist** will review the tissue sample collected from your previous brain biopsy or surgery done at another institution to confirm the diagnosis of low-grade glioma.
- A blood draw to test your **blood chemistry** (elements and minerals in your blood as well as a measure of how your liver and kidneys are functioning) and for a **complete blood count** with platelets and differential (a count of each type of blood cell). About 4 teaspoons of blood will be collected for this purpose.
- An **autoimmune assessment** will be done for research purposes only and would not be done if you were not taking part in the study. This is a blood draw to check if you have an autoimmune disorder (when your body attacks its own healthy cells). About 1 teaspoon of blood will be collected to test for antinuclear antibody (**ANA**), thyroid stimulating hormone (**TSH**), free thyroxine (**FT4**), and rheumatoid factor (**RF**).
- A blood draw to check if you have active or chronic **hepatitis B and C** (**HBsAg**, **HBsAb**, and **HBcAb**). This will be done for research purposes and would not be done if you were not taking part in the study.
- A blood draw for **HLA (human leukocyte antigen) typing**. This will be done for research purposes and would not be done if you were not taking part in the study. You must be HLA-A2 positive to take part in this study. HLA typing can be done at any time prior to study enrollment.
- Routine **urinalysis**, which is an analysis of your urine.
- Serum or urine **pregnancy test** if you are a woman of childbearing potential within 7 days prior to registration. This test must be negative in order for you to take part in this study.

The results of these tests will determine whether you are eligible to begin the study drugs. If you are not eligible, you will not be able to participate in the trial and your doctor will discuss alternative treatments with you.

During the main part of the study...

If the exams, tests, and procedures show that you are eligible to begin the study, and you choose to take part, the following procedures will happen:

This study has two study groups, ***Arm 1*** and ***Arm 2***.

Arm 1 will receive ***IMA950 and Poly-ICLC plus Varlilumab***.

- You will receive IMA950 and Poly-ICLC by injection followed immediately by a Varlilumab infusion (given through a vein) **-23 ± 2 days** (about 3 weeks) before the date of your scheduled standard-of-care surgery to remove your glioma.

- You will then receive IMA950 and Poly-ICLC by injection at the following time points leading up to your scheduled surgery: **-16 ± 2 days**, **-9 ± 2 days,** and **24-48 hours prior to surgery**.
- After surgery, you will continue to receive IMA950 and Poly-ICLC by injection every 3 weeks at the following time points: **Weeks A1, A4, A7, A10, A13, A16, A19, A22**; defining A1 as the week you receive your first vaccine after surgery. Week A1 will be at least 2 weeks after stopping your post-operative steroid and within 10 weeks of your surgery.
- After surgery, you will also continue to receive a Varlilumab infusion every 6 weeks immediately following your IMA950 and Poly-ICLC injection at the following time points: **Weeks A1, A7, A13, and A19**.

Arm 2 will receive ***IMA950 and Poly-ICLC ONLY***

- You will receive IMA950 and Poly-ICLC by injection **-23 ± 2 days** (about 3 weeks) before the date of your scheduled standard-of-care surgery to remove your glioma and at the following time points leading up to your surgery: **-16 ± 2 days**, **-9 ± 2 days,** and **24-48 hours prior to surgery**.
- After surgery, you will continue to receive IMA950 and Poly-ICLC by injection every 3 weeks at the following time points: **Weeks A1, A4, A7, A10, A13, A16, A19, A22**; defining Week A1 as the week you receive your first vaccine after surgery. Week A1 will be at least 2 weeks after stopping your post-operative steroid and within 10 weeks of your surgery.

VACCINE ADMINISTRATION

- Trained research staff at the UCSF Clinical Research Center will administer the vaccines.
- ***Both Arms 1 and 2***: A mixture of IMA950 and Poly-ICLC vaccine will be given by injection in the upper thigh.
- ***Arm 1 only:*** Varlilumab vaccine will be given by IV (infusion via vein) over 90 minutes immediately following the IMA950 and Poly-ICLC injection.
- You will remain in the Clinical Research Center and observed by research staff for one hour after vaccine administration.
- Trained research staff will assess your vaccine injection site 48 hours after the IMA950 and Poly-ICLC injection by phone or in-person.
- You will be asked to measure any changes at the injection site 48 hours after the injection using a transparency form provided by your doctors.

SAFETY LEAD-IN PHASE

The study begins with a "safety lead-in" phase to confirm the safety of the vaccines used in both Arms.

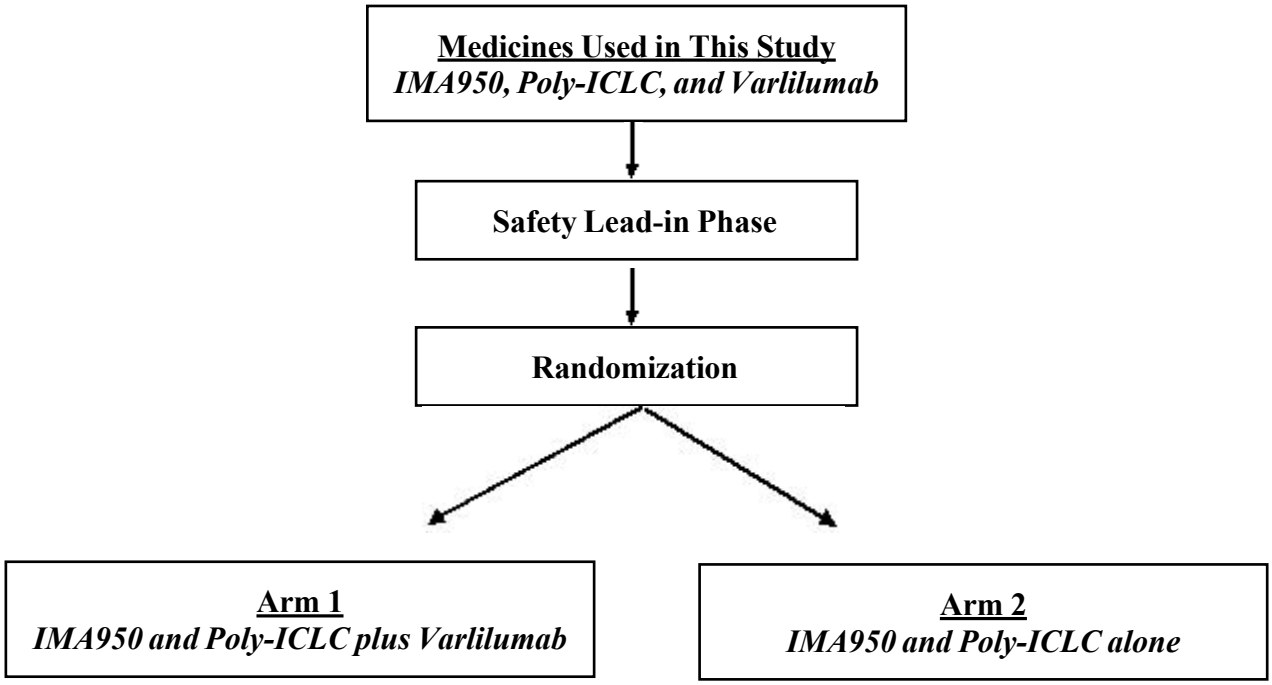
The first three patients enrolled in the study will be assigned to Arm 2 to confirm the safety of IMA950 and Poly-ICLC vaccine alone. ***Then the next three patients will be assigned to Arm 1*** to confirm the safety of IMA950 and Poly-ICLC plus Varlilumab vaccine.

There will be a review of the results of this safety lead-in phase before the study continues.

RANDOMIZATION

All patients enrolled in the study after the safety lead-in phase will be randomized to one of the two study groups, Arm 1 or Arm 2. Randomization means you will be assigned to a group by chance (like flipping a coin). Neither you nor your doctor can choose the group and you will have an equal chance of being placed in either group. You will be informed of which Arm you are assigned, but this will be randomly performed to a 1:1 ratio.

Your study doctor will tell you whether you will be in the safety lead-in phase or randomized to one of the study groups.



PRE-SURGERY STUDY PROCEDURES: -23 ± 2 days, -16 ± 2 days, -9 ± 2 days and 24-48 hours before surgery.

You will have the following procedures on the days you come to clinic for vaccinations before your scheduled standard-of-care surgery:

- Review of your **interval medical history** including any medications you are currently taking.
- **Physical and neurological examinations** including a **performance status** assessment (a measure of how well you are able to do your daily activities).
- Review of any **side effects** you may be experiencing.
- **Vital signs** before and one hour after vaccine administration.
- ***Both Arms 1 and 2*: Vaccination** with IMA950 plus Poly-ICLC by injection at the following time points leading up to your scheduled standard-of-care surgery to remove your glioma: **-23 ± 2 days, -16 ± 2 days, -9 ± 2 days,** and **24-48 hours before surgery**.
- ***Arm 1 only***: **Vaccination** with Varlilumab IV infusion over 90 minutes immediately following the IMA950 and Poly-ICLC injection **-23 ± 2 days** prior to surgery.

- Blood draw to test blood **chemistry** and for a **complete blood count** with differential and platelets (about 4 teaspoons).
- About 6 tablespoons of **research blood** will be drawn to test for substances that affect the body's immune system **-23 ± 2 days** prior to surgery, which is the day of your first vaccine.
- **Assessment of vaccine injection site 48 hours post-injection** by phone or in-person.
- You will be asked to **measure any changes to the injection site** using a transparency form provided by your doctors.

STANDARD-OF-CARE SURGERY: DAY 0

- Pre-operative **brain MRI** per standard-of-care to assess tumor growth.
- Part of the brain tumor removed during your surgery will be examined for **research** purposes, including to see whether the vaccine influenced your tumor tissue.
- **Research blood** samples will be collected during surgery to test for substances that affect the body's immune system (about 6 tablespoons).

STUDY PROCEDURES: POST-SURGERY

Within 14 days after your standard-of-care surgery, all patients enrolled will have the following tests and procedures, which will take about 1.5 hours to complete:

- **Post-operative brain MRI** should be complete within 14 days of surgery. MRI takes about one hour to complete.
- **UCSF pathology** will review the removed tumor to confirm that the tumor belongs to the type being studied in this research study (i.e., WHO grade II glioma).
- Review of your **interval medical history** including any medications you are taking.
- Review of your **expected date off dexamethasone** (post-operative steroid).
- **Vital signs** and **performance status** assessment.
- Review of any **side effects** you may be experiencing.
- A blood draw to test your **blood chemistry** and for a **complete blood count** with differential and platelets (about 4 teaspoons).

STUDY PROCEDURES: POST-SURGERY, WEEK A1

At least 2 weeks after stopping your post-operative steroid and within 10 weeks of your surgery, you will have the following tests and procedures:

- **Brain MRI** to assess the status of your tumor. If post-op MRI is greater than 14 days from A1 vaccine, then a new MRI will be done that is within 28 days of your post-op A1 vaccine should be complete within 14 days of your surgery and 28 days prior to your first vaccine.
- Review of your **interval medical history** including any medications you are currently taking.
- **Physical and neurological examinations** with a **performance status** assessment.
- Review of any **side effects** you may be experiencing.
- **Vital signs** before and one hour after vaccine administration.
- ***Both Arms 1 and 2*: Vaccination** with IMA950 and Poly-ICLC by injection.
- ***Arm 1 only***: Varlilumab by IV infusion over 90 minutes and a **research blood** draw before and 30 minutes after the end of the infusion (about 6 tablespoons). An additional sample of research blood will be drawn if you experience an infusion reaction.

- Blood draw to test blood **chemistry** and for a **complete blood count** with differential and platelets (about 4 teaspoons).
- **Research blood** draw to test for substances that affect the body's immune system (about 6 tablespoons).
- **Assessment of vaccine injection site 48 ± 2 hours post-injection** by phone or in-person.
- You will be asked to measure any **changes to the injection site** using a transparency form provided by your doctors.

STUDY PROCEDURES: POST-SURGERY, WEEKS A4, A7, A10, A13, A16, A19, A22

The following tests and procedures will be done every 3 weeks (± 7 days) after surgery unless otherwise noted:

- Review of your **interval medical history** including any medications you are currently taking.
- **Physical and neurological examination** including **performance status** assessment.
- Review of any **side effects** you may be experiencing.
- **Vital signs** before and one hour after vaccine administration.
- ***Both Arms 1 and 2:*** **Vaccination** with IMA950 and Poly-ICLC by injection at the following time points: **A4, A7, A10, A13, A16, A19** and **A22**.
- ***Arm 1 only***: Varlilumab by IV infusion and a **research blood** draw before and 30 minutes after the end of the infusion (about 6 tablespoons) at the following time points: **Weeks A7, A13,** and **A19**.
- Blood draw to test blood **chemistry** and for a **complete blood count** with differential and platelets (about 4 teaspoons).
- **Research blood** draw (about 6 tablespoons) to test for substances that affect the body's immune system at the following time points: **Weeks A13 and A19**.
- **Assessment of vaccine injection site 48 ± 2 hours post-injection** by phone or in-person.
- You will be asked to **measure any changes to the injection site** using a transparency form provided by your doctors.
- **Brain MRI** at **Week A10**.

STUDY PROCEDURES: WEEK A25

- Review of your **interval medical history** including any medications you are currently taking.
- **Physical and neurological examination** with **vital signs** and a **performance status** assessment.
- Review of any **side effects** you may be experiencing.
- A blood draw to test your blood **chemistry** and for a **complete blood count** with differential and platelets (about 4 teaspoons).
- A **research blood** draw to test for substances that affect the body's immune system (about 6 tablespoons).
- A research blood draw to check if you have active or chronic **hepatitis B and C** (**HBsAg**, **HBsAb**, and **HBcAb**). This will be done for research purposes and would not be done if you were not taking part in the study.
- **Brain MRI** to assess the status of your tumor.

- **ECG** if clinically necessary.

POST-VACCINE FOLLOW-UP

All patients, including those who discontinue the study early, will be followed for response and side effects until their tumor grows, they start a different treatment, or for up to 24 months from study registration (whichever comes first). Follow-up visits will be scheduled per standard-of-care (i.e., every 3 months).

You will have the following procedures performed post-vaccine at your doctor's recommendation:

- Review of your **interval medical history** including any medications you are currently taking.
- **Physical and neurological examination** with **vital signs** and a **performance status** assessment.
- Review of any **side effects** you may be experiencing.
- A blood draw to test your blood **chemistry** and for a **complete blood count** with differential and platelets (about 4 teaspoons) at the first follow-up visit only unless abnormal.
- **Brain MRI** to assess the status of your tumor.

The remaining follow-up will be conducted over the phone or by a medical record review every 3 months in order to assess your health condition.

How long will I be in the study?

You will continue to receive the study drugs as long as your cancer is stable and does not grow up to Week A25 or until one or more of the following events happen:

- Your cancer becomes worse
- You experience intolerable side effects
- You develop an illness that prevents further administration of the study drugs
- You decide to withdraw from the study
- The study is stopped
- You are a female who becomes pregnant

If you are removed from the research study, your study doctor will explain to you why you were removed.

Can I stop being in the study?

Yes. You may decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop the study. The study doctor will tell you how to stop your participation safely, evaluate any side effects you may be experiencing, and discuss what follow-up care and testing could be most helpful for you.

The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

What side effects or risks can I expect from being in the study?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the study medications. In some cases, side effects can be serious, long lasting, or may never go away. As with any investigational procedure, there may be adverse events or side effects that are currently unknown and certain of these unknown risks could be permanent, serious, life threatening, or even cause death.

You should talk to your study doctor about any side effects you experience while taking part in the study.

Risks and side effects from IMA950:

Likely

- Fatigue
- Fever
- Injection site reaction
- Itching
- Joint pain

Less Likely

- Decreased white blood cell count
- Rash

Rare but serious

- Allergic reaction
- Anaphylaxis (severe allergic reaction)
- Erythema multiform (severe skin reaction that may include rash and sloughing or death of tissue)
- Reactivation of viral infection

Risks and side effects from Poly-ICLC:

Likely

- Chills/rigors
- Fatigue
- Fever
- Flu-like symptoms
- Headache
- Injection site reaction
- Joint pain

- Local pain
- Malaise
- Pain, muscle

Less Likely

- Decreased white blood cell count (transient)
- Increased liver enzymes (ALT, AST, ALP)
- Nausea
- Swelling around tumor (transient)
- Vomiting

Rare but serious

- Seizures

Risks and side effects from IMA950 and Poly-ICLC mixture:

Likely

- Fatigue (lethargy, malaise, asthenia)
- Fever (in the absence of low white cell count)

Less Likely

- Decreased white blood cell count
- Headache
- Hives
- Increased liver enzymes (ALT, AST, ALP)
- Joint pain
- Muscle pain
- Rash
- Rigors/chills
- Swelling around brain tumor

Risks and side effects from Varlilumab:

VARLILUMAB (CDX-1127)

To date, varlilumab has been administered to approximately 370 patients with various types of cancers, and most side effects have been mild-to-moderate in intensity. Safety data is available from 343 patients, including 90 patients who were administered varlilumab alone and the remaining who received varlilumab in combination with another agent(s). Side effects attributed to varlilumab have included:

Frequent (occurring in >20% of patients)

- Fatigue
- Rash

Somewhat Frequent (occurring in 11-20% of patients)

- Itching

- Diarrhea
- Nausea

Less Frequent (occurring in 6-10% of patients)

- Infusion reaction with symptoms including chills, nausea, rash, hot flashes
- Decreased appetite
- Vomiting
- Headache
- Fever

A decrease in the lymphocyte count, a type of white blood cell, has commonly been observed following administration of varlilumab and has not been associated with symptoms.

Varlilumab has been given in combination with other drugs that activate the immune system called checkpoint inhibitors, specifically Opdivo (nivolumab), Tecentriq (atezolizumab), and Yervoy (ipilimumab). Immune-related side effects are expected with checkpoint inhibitors and have been observed among the 202 patients who have received varlilumab in combination with these drugs. Serious drug related immune-related side effects requiring hospitalization, such as inflammation of the digestive tract (colitis), inflammation of the liver (hepatitis), and inflammation of the lung (pneumonitis) have rarely occurred when varlilumab has been given in combination with checkpoint inhibitors. One patient who developed pneumonitis while being treated with varlilumab and nivolumab died from this side effect. However, the frequency of these side effects has not been greater than would be expected for the checkpoint inhibitors alone.

Rare but serious events:

- Bronchospasm (bronchospasm; wheezing)
- Inflammation of the kidney (acute kidney injury)

Additional side effects thought possible:

In laboratory tests, varlilumab has demonstrated the capacity to activate immune cells that are capable of destroying tumor cells. However, varlilumab may also activate immune cells that could cause side effects and/or damage to normal tissue.

Varlilumab induced activation of normal immune cells may cause symptoms during or shortly after finishing the varlilumab infusion. Such symptoms are called infusion reactions and as noted above, have occurred in approximately 8% of patients administered varlilumab. The infusion reactions have generally been mild and resolved with or without treatment. Other symptoms that can be associated with infusion reactions include low blood pressure, fever, shortness of breath, vomiting, abdominal pain, and rash; symptoms may be mild to moderate or could be severe and lead to life threatening complications such as renal failure, mental status changes and even death. Because varlilumab is a protein, it is also possible that you could have an allergic reaction to varlilumab with similar signs and symptoms as just described. Therefore, you will be monitored in the clinic for 1 hour after receiving the drug (the usual time frame in which these types of extreme reactions may develop), as well as throughout the study period.

Other types of immune activating antibodies have been tested in people and have had side effects ranging from mild to life threatening. Based on studies of other antibodies that activate the immune system in different ways, the following side effects might also be possible:

• Hair loss, loss of pigmentation (color) in the skin (vitiligo)

•Severe inflammation of the gastrointestinal tract (including severe diarrhea, passage of blood, abdominal pain, damage to the lining of the intestine, perforation of the intestine). These events may be serious or life threatening, and may require additional treatments such as treatment with corticosteroids, blood transfusions, intravenous artificial nutrition, and hospitalization. In some cases, sigmoidoscopy, colonoscopy (minimally invasive tests where your doctor inserts a scope in your rectum to look inside you colon or part of it) or surgery may be required.

•Changes in number of the various types of cells in the blood, such as neutrophils (which fight infection) and platelets (which make blood clot).

•Changes in functioning in the organs of the endocrine system: pituitary inflammation/failure (causing weight loss, fatigue, weakness, depression, loss of energy, nausea, vomiting, loss of appetite, and confusion; usually treatable but can rarely be fatal), over or under-activation of the thyroid (hypothyroidism or hyperthyroidism), adrenal insufficiency (if not treated, adrenal insufficiency may result in severe abdominal pains, diarrhea, vomiting, muscle weakness and fatigue, depression, extremely low blood pressure, weight loss, kidney failure, changes in mood and personality, and shock) and decreased function of the testes or ovaries (causing loss of sexual function/drive, muscle loss, sleep disturbance, mood/mental disorders, loss of bone mass, loss of hair, infertility and other symptoms)

•Inflammation of the eye (causing visual disturbances or pain)

Based on experience with other immune activating antibodies, it is expected that if events listed above were to occur, they would likely be quickly controlled with appropriate therapy. However, it is possible that side effects could potential rapidly worsen and become life-threatening and even cause death. Any delay in treating these side effects may prolong their duration, and make them more difficult to treat. **You should always report any new symptoms during your regular study visits, and immediately contact the study doctor if you develop any worrisome symptoms including the following:**

Diarrhea:

- An increase by 2 or more bowel movements a day above your normal pattern, especially if they wake you up at night or the urge to move your bowels comes on suddenly. Even if you are not feeling particularly unwell, DO NOT DELAY IN CONTACTING THE STUDY PHYSICIAN OR NURSE.
- ANY blood in the bowel movements, even if there is no diarrhea.
- ANY marked change in bowel habits, either new constipation or diarrhea.

Abdominal (Stomach) pain or tenderness:

- Even if there is no diarrhea, and particularly if the pain is associated with a fever or requires the use of pain medications. Note: narcotic pain relievers used for abdominal (stomach) pain can suppress diarrhea or symptoms of other adverse events – please check with the study physician or nurse before using for abdominal (stomach) pain.

For patients with tumors that express CD27 (found in some cancers of the blood), it is possible that varlilumab could rapidly kill the tumor cell and cause something called tumor lysis syndrome. This is unlikely to happen with varlilumab but if it were to occur it could cause changes in laboratory tests without any associated symptoms, or in severe cases, damage to the kidney or other organs.

It is theoretically possible that varlilumab could cause leukemia or lymphoma malignancies that express CD27 to grow and therefore worsen the clinical situation. Another theoretical possibility is that varlilumab may kill normal CD27 expressing immune cells that could result in an increased risk for developing infections, including potentially life-threatening infections. It is unlikely that these theoretical risks will actually occur because they have not been observed in testing with varlilumab, including in animal studies.

If you were to require prolonged treatment with immunosuppressive medications, such as corticosteroids, to manage a serious side effect associated with varlilumab and/or IMA950 vaccine and polyICLC (Hiltonol), your body's ability to fight off certain infections (i.e., opportunistic infections) may be lowered. These infections may require treatment with antibiotic or antifungal medications and may be fatal.

Varlilumab combined with IMA950 vaccine and polyICLC (Hiltonol),

Varlilumab combined with IMA950 vaccine and polyICLC (Hiltonol), for the treatment of advanced solid tumors has not been studied in another clinical trial. The side effects of the combination may be similar to what has been identified in other trials separately evaluating varlilumab or IMA950 vaccine and polyICLC (Hiltonol), or the side effects of the combination may be different. There also may be new side effects of the combination that are not yet known that may occur. You should tell your doctor or nurse right away about any possible side effects you experience with this combination treatment.

A small percentage of patients in this study may experience tumor "***pseudo-progression***," which is defined as transient (lasting only for a short time) worsening of clinical and/or imaging findings due to inflammatory responses in the tumor induced by immunotherapy. While true progression means growth of tumor cells, "pseudo-progression" is attributed to a therapeutic response. Patients with pseudo-progression have shown enlargement or appearance of new contrast enhancement of tumor on MRI. Patients may also present with transient clinical signs that are similar to ones seen in tumor progression, such as headaches, increased sleepiness, weakness, and seizures. It may be challenging to distinguish true vs. pseudo-progression because there are no specific signs for pseudo-progression. When pseudo-progression is suspected, your doctor will carefully observe your condition, and may give you a small dose of corticosteroid, which usually alleviates the inflammatory response and or symptoms; then your doctor will order a follow-up MRI scan in order to closely monitor you and ensure that you improve with continued management.

Any cases of suspected tumor progression or pseudo-progression will be carefully reviewed by study investigators to determine whether the patient should remain in the trial. In addition, pseudo-progression that necessitates hospitalization and treatment for more than 72 hours will be considered a regimen-limiting toxicity.

Randomization Risks

You will be assigned to a study group by chance, and the study drugs you receive may prove to be less effective or to have more side effects than the other study drug regimen.

Blood Drawing (Venipuncture) Risks

Drawing blood may cause temporary discomfort from the needle stick, bruising, infection, and fainting.

Risks associated to Hepatitis testing

Being tested for hepatitis may cause anxiety regardless of the test results. A positive test result means that you have been infected with the hepatitis virus, but no one can say for certain when, if ever, you will become sick. Receiving positive results may make you very upset. If other people learn about your positive test results, you may have trouble obtaining insurance or employment. If your test is negative, there is still the possibility that you could be infected with the hepatitis virus and test positive at some point in the future. There is always the possibility that the test results could be wrong.

MRI Risks

Because the MRI machine acts like a large magnet, it could move iron-containing objects in the MRI room during your examination, which in the process could possibly harm you. Precautions have been taken to prevent such an event from happening; loose metal objects, like pocket knives or key chains are not allowed in the MRI room. If you have a piece of metal in your body, such as a fragment in your eye, aneurysm clips, ear implants, spinal nerve stimulators, or a pacemaker, you will not be allowed into the MRI room and cannot have an MRI.

Having an MRI may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia and by the loud banging noise during the study. Temporary hearing loss has been reported from this loud noise. This is why you will be asked to wear earplugs. At times during the test, you may be asked to not swallow for a while, which can be uncomfortable.

Because the risks to a fetus from MRI are unknown, pregnant women must not participate in this study.

Contrast Agent (Gadolinium) Risks

A few side effects of gadolinium injection such as mild headache, nausea, and local pain may occur. Rarely (less than 1% of the time) low blood pressure and lightheadedness occurs. This can be treated immediately with intravenous fluids. Very rarely (less than on in one thousand), patients are allergic to gadolinium. These effects are most commonly hives and itchy eyes, but more severe reactions have been seen which result in shortness of breath.

Patients with severe kidney disease sometimes have a bad reaction to gadolinium contrast. The condition is called nephrogenic systemic fibrosis (NSF). It can cause skin to tighten or scar and can damage internal organs. Sometimes it can be life-threatening. There are no reports of NSF in

patients with normal kidney function. Before you have a MRI scan requiring an injection of gadolinium contrast, you will have a blood test in order to check the function of your kidneys. Based on your medical history and the results of the test, a doctor will decide whether it is safe for you to undergo the MRI scans.

Risks associated to ECG

A 12-lead ECG, or electrocardiogram, involves placing electrodes on the skin. You may experience an allergic reaction to the adhesive used to attach the electrodes to the skin. These symptoms are generally mild and clear up on their own. Please let your doctor know if you are aware of any allergies.

Reproductive Risks

Women who are pregnant or breastfeeding cannot take part in this study, because the study drugs may affect an unborn baby or be passed to a baby through mother's milk. If you are a woman capable of having children, you will be given a pregnancy test within 7 days before you begin the study, and the results must be negative for you to participate. Also, if applicable, breastfeeding must be discontinued while you are on this study and for a week after taking the last dose of study drugs.

Due to the unknown effects of agents that help fight cancer therapies on an unborn fetus, it is very important that you (for female participants) or your female partner (for male participants) do not get pregnant during participation in this study. Avoiding sexual activity is the only certain method to prevent pregnancy. However, if you choose to be sexually active, you must agree to use an appropriate double barrier method of birth control (such as female use of a diaphragm, intrauterine device [IUD], sponge and spermicide, in addition to the male use of a condom) or a prescribed birth control implant. Both double barrier contraception and implants must be used for at least one week prior to the start of the research study and continue for at least two weeks following the last study visit. It is important that you discuss your method of birth control with your doctor prior to starting the study. If you plan to change your birth control method while you are on the study, you must notify your doctor before doing so.

If you choose to be sexually active during this study, you must accept the risk that pregnancy could still result, exposing you or your sexual partner to potential loss of pregnancy as well as other unknown effects on the developing fetus. If you (a woman) become pregnant or if you (a man) impregnate a woman while you are taking part in this study, you must notify one of the doctors listed on this form immediately so that management of the pregnancy and the possibility of stopping the study drugs can be discussed.

Breach of Confidentiality Risk

There is a possibility that if the results of the research studies involving your biological material were to become generally known this information could impact future insurability, employability, or reproduction plans, or have a negative impact on family relationships, and/or result in paternity suits or stigmatization. The research staff will take all necessary steps to ensure that this does not happen, including but not limited to removing your identifying information from reports, keeping your records in a locked file room, and using passwords for computer files.

There is a small risk of a breach of confidentiality occurring, which would entail the unauthorized or inappropriate sharing or release of your medical or research data.

Unknown Risks

The experimental study drugs may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

What are possible benefits from taking part in this study?

Taking part in this study may or may not make your health better. While the study doctors hope that the study drugs will be more useful against cancer compared to the usual treatment, there is no proof of this. We do know that the information from this study will help doctors learn more about these study drugs as a treatment for cancer. This information could help future cancer patients.

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

If you do not wish to take part in this research study, your doctor will discuss alternate standard- of-care treatment options with you, including their benefits and risks. These may include:

- Getting treatment or care for your cancer without being in a study. This may include treatment with surgery alone or in combination with chemotherapy and/or radiation therapy.
- Taking part in another research study.
- Getting treatment for your symptoms only, with no further cancer therapy. This is called comfort care, or palliative care. This type of care helps reduce pain, tiredness, appetite problems, and other problems caused by the cancer. In comfort care, treatment is not directed at curing, slowing, or reversing your disease, but tries to improve how you feel and tries to keep you as active and comfortable as possible.

Except for surgery, there is no firmly established standard-of-care for WHO grade II glioma. While radiation therapy is often used to treat these tumors, it is not clear whether radiation therapy should be used at first diagnosis or after the tumor regrows. Studies have demonstrated the benefits of radiation therapy plus chemotherapy compared to radiation therapy alone for patients with newly diagnosed WHO grade II glioma. Patients are entitled to pursue radiation therapy or radiation therapy plus chemotherapy as alternatives to this clinical trial.

Talk to your study doctor and personal doctor about each of these choices before you decide if you will take part in this study. If you decide not to participate, withdraw your participation after starting the study, or if you are discontinued from this study, your doctor will discuss all other treatment options with you.

How will information about me be kept confidential?

Any information about you obtained from this research will be kept as confidential (private) as possible but we cannot guarantee total privacy. Some information from your medical records will be collected and used for this study. If you do not have a UCSF medical record, one will be created for you. Your signed consent form and some of your research tests will be added to your UCSF medical record. Therefore, people involved with your future care and insurance may become aware of your participation and of any information added to your medical record as a

result of your participation. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

All records related to your involvement in this research study will be stored in a locked file cabinet and on a secure computer server. Your identity on these records will be indicated by a case number rather than by your name, and the information linking these case numbers with your identity will be kept separate from the research records.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- University of California
- National Cancer Institute
- U.S. Food and Drug Administration (FDA)
- Immatics, Inc.
- Oncovir, Inc.
- Celldex Therapeutics, Inc.

California Confidentiality Statement

Hepatitis B and C Reporting: California regulations require laboratories to report new cases of hepatitis B and hepatitis C infection to the county public health department. The reports include the patient's name, social security number, and other identifying information. Information about these new infections is used to track these diseases statewide and nationwide. Other than this required reporting, your results will be treated confidentially by the study staff. Personally identifying information will not be reported to other departments or agencies.

What are the costs of taking part in this study?

Two types of procedures will be done during this study. Some are part of your standard medical care and others are only for research. You or your insurer will be billed for the standard medical care. You will be responsible for your co-pays, deductibles, and any other charges that your insurer will not pay. There is a possibility that your insurer may not cover all standard medical care costs if you are receiving medical services out of network. Any procedures done only for research will not be charged to you or your insurer.

Some of the services you will receive are being done only because you are participating in this research study. These services will be paid for by the study and will not be billed to you or your health insurance company. These "research only" services include the following:

- Autoimmune assessment, hepatitis and pregnancy testing, and routine urinalysis
- Examination of tumor tissue removed during surgery for research purposes
- Research-related blood tests
- Vaccine and vaccination
- ECG

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's web site at http://cancer.gov/clinicaltrials/understanding/insurance-

coverage. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call **1-800-4-CANCER (1-800-422-6237)** and ask them to send you a free copy.

Will I be paid for taking part in this study?

You will not be paid for taking part in this study.

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

It is important that you tell your study doctor, Dr. Nicholas Butowski, and/or the study team if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him [redacted] or call the RN main line [redacted].

> **Treatment and Compensation for Injury:** If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California depending on a number of factors. The University does not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Committee on Human Research at (415) 476-1814.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?

You can talk to your study doctor and/or study team about any questions, concerns, or complaints you have about this study. Contact your study doctor, Dr. Nicholas Butowski, [redacted] or call the RN main line [redacted]

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers, or if you wish to voice any problems or concerns you may have about the study, please call the Office of the Committee on Human Research at 415-476-1814.

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.

CONSENT

You have been copies of this consent form and the Experimental Subject's Bill of Rights to keep. You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

If you wish to participate in this study, you should sign below.

_____
Printed Name of Participant

_____ _____
Participant's Signature for Consent Date

_____ _____
Signature of Person Obtaining Consent Date

_____ _____
Witness – (Only required if the participant is a non-English speaker) Date