Study Title: ATTAC-II: A Phase II Randomized, Blinded, and Placebo-Controlled Trial of CMV RNA Pulsed Dendritic Cells with Tetanus-Diphtheria Toxoid Vaccine in Patients with Newly-Diagnosed Glioblastoma

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UF UNIVERSITY of FLORIDA
The Foundation for The Gator Nation

INFORMED CONSENT FORM
to Participate in Research, and

AUTHORIZATION
to Collect, Use, and Disclose Protected Health Information (PHI)

INTRODUCTION

If you are a legally authorized representative for the subject, as you read the information in this Consent Form, you should put yourself in their place to decide whether or not to allow us to collect research information about them and to allow them to take part in this study. If the subject you are representing becomes able to understand the information in this Consent Form while they are still participating in the study, he/she must then decide on their own if he/she wants to continue to take part in this research study. As you read the rest of this form, the word "you" refers to the subject.

Name of person seeking your consent:_____

Place of employment & position: _____

Please read this form which describes the study in some detail. A member of the research team will describe this study to you and answer all of your questions. Your participation is entirely voluntary. If you choose to participate you can change your mind at any time and withdraw from the study. You will not be penalized in any way or lose any benefits to which you would otherwise be entitled if you choose not to participate in this study or to withdraw. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 273-9600.

GENERAL INFORMATION ABOUT THIS STUDY

1. Name of Participant ("Study Subject")

_____

2. What is the Title of this research study?

ATTAC-II: A Phase II Randomized, Blinded, and Placebo-Controlled Trial of CMV RNA-Pulsed Dendritic Cells with Tetanus-Diphtheria Toxoid Vaccine in Patients with Newly-Diagnosed Glioblastoma

3. Who is paying for this research study?

The sponsor of this study is the University of Florida Department of Neurosurgery.

4. Why is this research study being done?

Agreeing to become involved in any research is always voluntary. By signing this form, you are not waiving any of your legal rights. If you decide not to participate in this research, you will not be penalized in any way and you will not lose any benefits to which you are entitled. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 273-9600.

a) In general, what is the purpose of the research, how long will you be involved?

The purpose of this research study is to determine if an investigational vaccine made from your own cells, called pp65 DC, is effective for the treatment of glioblastoma (GBM) brain tumor when given with stronger doses of routine chemotherapy.

The use of a vaccine that activates your immune system is a type of immunotherapy. It is hoped that by giving the vaccine as a shot under the skin, the immune system will be activated to attack tumor cells in the brain while leaving normal cells alone.

The pp65 DC vaccine is investigational which means that it is not approved by the United States Food and Drug Administration (FDA) and is being tested in research studies.

You are being asked to be in this research study because you have been newly-diagnosed with glioblastoma.

Treatment with study drug will continue until 10 doses are given over the course of about 9 months.

b) What is involved with your participation, and what are the procedures to be followed in the research?

The following will be done to assess your eligibility and to conduct the study:
- Blood test for eligibility and safety monitoring during the study participation.
- Brain MRIs to evaluate your disease and groin MRIs (which is the study drug injection site) for research purposes.
- You will receive the following medications:
    - Chemotherapy: Temozolomide (TMZ) will be given as part of your normal care,

- Vaccination with Tetanus Diphtheria to boost your immune system, and
- Study vaccine or placebo.

- To make the study vaccine we will collect your white cells by performing a procedure called “Leukapheresis”. The procedure will take about 4-6 hours to complete and will require having venous access lines (similar to infusion lines) placed on each arm. The blood is drawn from one arm, the cells are filtered and the blood is returned through the other arm. If the veins in your arms are difficult to locate or to draw from, you will have a central line placed by physician in a large vein (e.g. in your neck or groin). Placement of a central line may require a procedure (similar to an operation). The doctor performing the procedure may use special x-rays to assist with placement of the special IV. The central line will be removed after the cell collection is complete. Two or more leukapheresis procedures will be needed to produce 10 vaccines.

Once made, the study vaccine will be given with monthly cycles of TMZ. In this study, you will take a higher dose of TMZ unless you are 70 years old or older. You will receive three vaccines during the 1st cycle of chemo, then monthly vaccination will continue until you receive 10 vaccines. If your disease worsens before you receive the 10 vaccines, you will no longer receive the study drug and your treating neuro-oncologist will discuss the best treatment options available.

c) What are the likely risks or discomforts to you?

Normal side effects and discomforts are expected due to the treatments and procedures. The risk related to the study drug and study procedures are listed below:

Study Drugs (pp65 DC Vaccine and PBMCs):

- Allergic reaction, swelling of the brain, infection and delayed autoimmune response.

Leukapheresis:

- Light-headedness, fainting, vomiting, rapid breathing, chills, tingling, and nausea, blood clots.
- You may need a special large IV placed in order to have leukapheresis. Placement of large IV in your arm or a central vein (like your neck or groin) include discomfort/pain, bruising, bleeding, and very rarely, injury to adjacent organs. The doctor placing the special IV will discuss these risks with you and you will sign a separate procedural informed consent form.

The risks and discomforts associated with participation in this trial are described in more detail later in this document.

d) What are the likely benefits to you or to others from the research?

The study vaccine may allow your immune system to better fight your tumor; however, it is possible that you will not benefit from taking part in this study.

Information gained from this study may help doctors advance the medical treatment for brain tumors.

e) What are the appropriate alternative procedures or courses of treatment, if any, that might be helpful to you?

If you do not want to be in this study, treatment may include surgery, radiation therapy with TMZ, and monthly cycles of TMZ, participation in another research study, if one is available and you qualify, or you can choose to have no treatment.

Additional and more detailed information is provided within the remainder of this Informed Consent form, please read before deciding if you wish to participate in this study

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by US 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.

WHAT CAN YOU EXPECT IF YOU PARTICIPATE IN THIS STUDY?

5. What will be done as part of your normal clinical care (even if you did not participate in this research study)?

If you chose not to participate in this research study, your normal clinical care would include the following 3 phases of treatment: 1) Surgery; 2) Radiation therapy with temozolomide; and 3) Monthly cycles of temozolomide.

Surgery
You would have surgery to remove as much of the tumor as possible.

Radiation therapy with temozolomide
After recovering from surgery, you would receive radiation therapy with temozolomide. One radiation treatment would be given daily, 5 days per week, for 6 total weeks. Temozolomide, a chemotherapy medication taken by mouth, would be taken once each day, including weekends, until the last radiation treatment. Throughout your treatment, you would be evaluated by your physician, have routine laboratory blood tests, and have a brain MRI (or CT scan if you cannot have an MRI) every 2-3 months to see if the tumor has returned or grown.

An MRI is a type of scan which uses a magnet, radio waves, and computer equipment to produce images of structures in your body. It is a large machine with a hole in the middle that looks like a doughnut with a table going through it. During the MRI, the magnet makes tapping, thumping, or other loud noises. Earplugs or music may be provided to help muffle or block the noise.

Monthly cycles of temozolomide

About 1 month after radiation therapy with temozolomide, you would start monthly temozolomide. You would take temozolomide once each day for 5 straight days every 28 days; this 28-day period is called a cycle. Treatment with temozolomide would continue for 6-12 cycles, provided you are able to tolerate the temozolomide and your tumor has not returned or grown. Throughout your treatment, you would be regularly evaluated by your physician, have routine laboratory blood tests, and have a brain MRI (or CT scan if you cannot have an MRI) every 2-3 months to see if the tumor has returned or grown.

6. What will be done only because you are in this research study?

If you decide to participate in this study, some of the study procedures will be performed only at UF Health, as described below.

Before you begin the study:

The study doctor or study staff will talk to you about the study to determine if you are willing to participate. Study procedures cannot begin until you give your permission by signing this consent form.

Enrollment Visit

If you agree to participate and after you sign the consent form, additional testing will be done to determine if you are eligible to enroll in the study.

We will collect information on your past and current medical history to determine eligibility. The physician or the nurse practitioner will perform a physical and neurological exam. If you are 50 years of age or older, we will perform a brief exam to assess how your brain processes the information.

Blood tests to check if you have ever been infected with any viruses that can be transmitted through the blood will also be done, including tests for HIV, Hepatitis B, Hepatitis C, and Cytomegalovirus (CMV).

A positive HIV test means that your blood sample tested positive for HIV and that repeat testing will be performed to confirm (prove) this finding. If your sample is positive for HIV, it means that you are a carrier of HIV and that you can pass the virus to others by intimate sexual contact, by sharing needles, and through donating blood and organs. A negative HIV test means that no antibody to HIV was found in your blood sample based on the result of the initial screening test, repeat screening tests, or a confirmatory test.

There can be individuals who have HIV test results that are called “false positive” (for some reason, the test indicates that HIV antibodies are present in the blood when they are not). There can also be false negative results which can have two possible meanings; the person has been infected with HIV, but that person’s body has not yet made antibodies to the virus, or HIV antibody is present in the person’s blood, but for some reason the test failed to detect it.

A member of the study team will meet with you before and after the HIV test. You may be asked to sign a separate consent form to have your blood tested for HIV. Because we will test your blood for HIV (the virus that causes AIDS), Florida Law requires that we tell you that:

- Your identity and HIV test result will be kept confidential to the extent provided by law.
- Any physician who performs an HIV test that has a positive result or lab that processes a blood sample for HIV that has a positive result must report this information to County Health Department with information that will identify you.
- If you want to get tested for HIV outside of this study, test sites that keep your results anonymous are available. You can contact the County Health Department for information on those sites.

If you test positive for HIV, we will do the following:

- Confirm the result by sending a sample of your blood for another HIV test.
- If the second test result is positive, the positive test result and your identity will be reported to the County Health Department. Florida law requires that we report this information.
- Provide information on medical and support services available to you; and
- Discuss information on the importance of notifying previous and current sexual partners that they may have been exposed to HIV and how to prevent HIV transmission.

If infected with HIV or Hepatitis, you will not be able to participate in this study. Also, if you are a female and able to become pregnant, we will perform a pregnancy test. If the results show that you are pregnant, you will not be able to participate in this study. You will also be informed of any other findings that would exclude you from participating in this study.

If you are not eligible, your study participation will end. You will not receive study drug. Your doctor will discuss appropriate standard treatments for you at that point.

Study Group Assignment:

If you are eligible to continue in the study and before leukapheresis to collect blood cells to make study drug, you will be assigned into a treatment group, however you will not receive your first dose of study drug until after you complete standard treatment with radiation and temozolomide. Study group assignment is done randomly (by chance) and is similar to the tossing of a coin. Neither you nor your study doctor can decide which group you are assigned to. In addition, your study group assignment is blinded;

meaning you will not know which study group you are in, or what treatment you are receiving. This is done to prevent any bias so that the results of the study can be presented in a fair manner.

You will be randomly assigned into one of three study drug groups:

Group 1: Experimental arm: pp65 DC vaccine (short) with GM-CSF and tetanus and diphtheria (Td)

Group 2: Experimental arm: pp65 DC vaccine (long) with GM-CSF and tetanus and diphtheria (Td)

Group 3: Placebo arm: Peripheral blood Mononuclear Cells (PBMCs) and saline skin preparation

You will have an equal (1 out of 3 or 33%) chance of being assigned to one of the study drug groups above.

pp65 DC short vaccine and pp65 DC long vaccine are both active study drugs. The difference between these 2 vaccines is the length of the pp65 protein. We do not know if the response to the pp65 DC short vaccine and pp65 DC long vaccine will be different. The responses to both vaccines will be measured during this research study and compared to each other. Peripheral blood mononuclear cells (PBMCs) that are collected by leukapheresis, will be used in this study as a placebo. The placebo will look like and will be given in the same way as the pp65DC vaccine, but it will not contain the same cells. The placebo will be used in this study to show what effect the pp65 vaccine has compared to no vaccine at all. If you are assigned to receive PBMCs, you will not receive the benefits of the pp65 DC vaccine, if there are any.

Td is a vaccine that is routinely given to protect individuals from tetanus and diphtheria, infections caused by bacteria. You will receive a Td booster before you get your first dose of study drug regardless of which group you are assigned. In this study, Td skin preparation will be given to help the vaccine boost your immune system.

The saline skin prep will be used in this study as a placebo. The placebo will look like and will be given in the same way as the Td skin prep but it will not contain the same ingredients. The placebo will be used in this study to show what effect the Td skin preparation has on boosting your immune system compared to no skin prep at all. If you are assigned to receive the saline skin prep, you will not receive the benefits of the Td skin prep, if there are any.

<u>Leukapheresis:</u>
After recovering from surgery and before radiation therapy with temozolomide, you will undergo a procedure called leukapheresis. The purpose of leukapheresis is to collect large numbers of white blood cells from your blood and use them to make the study drugs. All study participants will undergo all leukapheresis procedures at UF Health.

Before the leukapheresis procedure, you will have a clinic visit at UF Health that will include a physical examination and blood tests. Approximately 2 tablespoons, or 30cc,

of blood will be collected to check your blood counts, organ function, and electrolyte, or mineral, levels. Blood tests for HIV, Hepatitis B, Hepatitis C, Syphilis, and Cytomegalovirus (CMV) will be repeated. If you are a woman and able to have children, your blood will be tested to make sure you are not pregnant. If you are infected with HIV or Hepatitis or you are pregnant, your study participation will end and you will not receive study drug.

Next, you will undergo leukapheresis. In order to perform the procedure, a large needle (about the size of a sharpened pencil tip) will be placed in a vein in each arm. After placing the needles, blood will be taken from one needle and continuously processed through a machine called a cell separator. This machine is designed to remove some of your white blood cells. The remainder of your blood will be returned to you through the needle in your other arm. During the procedure, you will be asked to remain as still as possible. The total time required to complete leukapheresis is approximately 4-6 hours. If the veins in your arms needed to perform the leukapheresis are difficult to locate or to draw from, you will have a separate procedure by physician to insert a temporary central line placed in a large vein either in the neck (the jugular vein) or in the groin (the femoral vein). The doctor placing the line may use x-ray (called fluoroscopy) to assist with IV placement in the vein. This involves quick, low amounts of radiation. The doctor placing the line will explain the procedure and the risk and benefits associated with it and you will be asked to sign a separate consent form. The central line will be removed after the cells collection is complete. Pressure will be applied at the catheter insertion location for 5-10 minutes (maybe longer) and an occlusive bandage will be applied.

The leukapheresis procedure will be repeated about 1 month after your third dose of study drug so that more white blood cells can be collected to make more study drug. If we were not able to make enough vaccines from the 2 leukapheresis procedures, you may undergo additional leukapheresis to complete the study.

Radiation and Temozolomide:
Following leukapheresis, you will undergo treatment with standard radiation and temozolomide as described in Section 6 above. After you complete radiation therapy with temozolomide, the study doctor will determine if you are eligible to continue in the study based on how much temozolomide and radiation you received and blood test results. If you are not eligible, your study participation will end and you will not receive study drug.

If you are eligible to continue in the study, you will begin monthly cycles of temozolomide and scheduled study vaccines as described below.

Temozolomide:
About 4 weeks after you complete radiation therapy with temozolomide, you will begin monthly cycles of temozolomide. In this study, you will take a higher dose of temozolomide once each day for 21 straight days every 35 days. If you are 70 years or older, you will receive the standard dose of temozolomide for 5 straight days every 35 days. The number of days you receive temozolomide and the dose you receive may

be changed by your physician if you experience side effects or have problems with your laboratory blood test results.

Throughout your treatment with temozolomide, you will have routine monitoring as described in Section 6 above.

Study Drug Administration:

Study drug will be given in combination with your monthly temozolomide cycles. The first dose will be given 1-3 days after completion of your first temozolomide cycle (day 22-24). The second dose will be given two weeks later and the third dose will be given two weeks after the second dose. Starting with the fourth dose, study drug will be given on day 22-24 of each temozolomide cycle. The fourth dose of study drug will be given after your second leukapheresis with cycle two of temozolomide. All doses of study drug will be given at UF Health during study drug visits described below. If you cannot or do not want to travel to the University of Florida for these visits, you will not be able to participate in this study.

Treatment with study drug will continue until a total of 10 doses are given. 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 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.

At the time of each vaccination, if fewer cells are available in the study drug than the target dose, you will still receive a vaccination with the available number of cells. It is not known if giving a lower number of cells in the study drug makes a difference in how well the vaccine works. Based on the information we have, there is not a clear relationship between number of dendritic cells in the study drug and effectiveness of the vaccine. We believe that it is reasonable to give each dose of vaccine with the number of dendritic cells that are available. Using a lower number of dendritic does not change the risks of giving the vaccine. You will always be informed if less than the target number of dendritic cells is being given with any vaccination.

The following procedures will be performed at study drug visits at UF Health:

- You will receive a Td booster shot in the muscle of the upper arm before study drug dose #1 only. If you have received a Td booster shot in the past, you will still receive a Td booster shot before dose #1.
- You will receive the study drug as an injection just under the skin in both groin areas. Each injection will only take a few minutes and you will be monitored for 30 minutes to 1 hour after each injection to be certain you do not have a reaction.
- You will receive the skin prep as an injection just under the skin in both groin areas 6-24 hours before doses #3, #6, and #9.
- Blood will be drawn to learn more about the way the immune system is working in your body and the effects of the treatment. Blood (no more than 6 tablespoons or 90cc) will be collected at each of the following time points:
    - With the 1st leukapheresis
    - Before study drug doses #1, #2, and #3

- 48 hours and 5-7 days following study drug dose #3
- With the 2nd leukapheresis
- Before study drug doses #4, #7, and #10
- Anytime there is suspicion that your tumor may have returned or grown.

- A sample of your urine will be collected before you receive study drug dose #1 and before the skin prep injection, 48 hours and 5-7 days following study drug dose # 3.
- We will ask you about any medications you are taking and if you are having any side effects.

When you return to the clinic at UF Health before study drug dose #3, we will track where the study drug travels in the lymph nodes of your body by taking MRI (Magnetic Resonance Imaging)/MRS (Magnetic Resonance Spectroscopy) images of your groin. MRS is a type of scan similar to MRI which uses a magnet, radio waves, and computer equipment to produce images of the chemical content of tissue in your body. We will take these images and a sample of your urine before the skin prep injection, 48 hours and 5-7 days (optional) following study drug dose # 3.

If you are a woman and able to have children, your urine will be tested before the MRI/MRS to make sure you are not pregnant.

Tests done only for research purposes will not be evaluated or used to diagnose or treat any of your medical problems. These tests may need to be repeated if required for your medical care in the future.

After completing treatment, we will collect information on how you are doing and if your tumor has returned or grown. This information will be collected from your medical records or by contacting you by telephone every 2-3 months for as long as you allow us to do so.

It is possible that you become ineligible to receive the study drug during your participation in the study. For example if you cannot complete the full treatment of chemo-radiation, or if your chemo treatment is delayed for an extended time due to side effect or other unexpected events. In such case, you may receive the vaccines that are available if the study physician and the principal investigator believe you could benefit from getting the vaccines and that it is safe for you. However, no additional vaccines will be generated.

If the study physician decides you will benefit from starting another treatment, you will not receive the study vaccines.

Once this research study is completed, any information that could identify you **might** be removed from any identifiable private information or identifiable biospecimens collected and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative.

If you have any questions now or at any time during the course, please contact one of the research team members listed in question 1 of the addendum.

7. How long will you be in this research study?

Treatment with the study drug will continue until a total of 10 doses are given over the course of about 9 months. After that, we would like to collect information on how you are doing for as long as you allow us to do so.

8. How many people are expected to take part in this research study?

Approximately 200 people will take part in this study at the University of Florida, Orlando Health Cancer Institute and Duke University. Up to 125 subjects may enroll at the University of Florida.

WHAT ARE THE RISKS AND BENEFITS OF THIS STUDY AND WHAT ARE YOUR OPTIONS?

9. What are the possible discomforts and risks from taking part in this research study?

While in this study, you are at risk for possible side effects from the study drug and the study procedures. You should discuss these with the study doctor. The known side effects are listed below, but they will vary from person to person. There may also be other side effects that you experience that were not predicted. Many side effects go away shortly after the study drug is stopped, but in some cases, side effects may be serious, long lasting, and/or permanent and may even cause death.

Side effects that may be associated with some of the procedures used in this study are as follows:

Study Drugs (pp65 DC Vaccine and PBMCs):
Allergic reaction: The study drug may cause an allergic reaction, which could include pain, redness or swelling at the injection site, itching, hives, low blood pressure, difficulty breathing, or in the most extreme circumstances, death.

Cerebral edema or swelling of the brain: Cerebral edema may be caused by the tumor, surgery, radiation, immune cells in the brain, or the killing of tumor cells. Symptoms of cerebral edema may include severe headache, confusion, lack of energy, unconsciousness, coma, or loss of movement, sensation or function of certain areas of the body. You will be monitored for signs of cerebral edema throughout the study and treated if necessary. Cerebral edema that does not respond to treatment may lead to permanent damage.

Infection: If the study drug comes in contact with something unclean (contaminated) when it is being made, it could cause an infection. An infection may cause redness, swelling, and/or uncomfortableness at the injection site. In extreme cases, this could lead to a severe infection of the blood (sepsis) and possibly death. The risk of infection is very low because the study drugs are made in a special laboratory with strict rules and they are tested for germs. You will be monitored for signs of infection throughout the study and treated if necessary.

Delayed autoimmune disease: The study drug may activate the immune system to such a high degree that the immune system may start to attack normal brain tissue or other tissues in the body.

Td Booster and Td Skin Prep:
Side effects that may be caused by Td include:

- pain, tenderness, redness, hardness, itching, swelling, and/or warmth at the injection site
- swelling of the arms and/or legs
- fever and/or flu-like symptoms
- dizziness, headaches, and/or convulsions (sudden, violent shaking of the muscles)
- muscle, joint, and/or bone stiffness and/or pain
- rash
- nausea
- cellulitis, an infection of the skin

Rarely, severe shoulder pain and reduced movement in the arm where the shot was given can happen. Severe allergic reactions that cause redness or swelling at the injection site, itching, hives (raised red and sometimes itchy spots on the skin), low - blood pressure, difficulty breathing, or death, are very rare. Rare cases of Guillain-Barré syndrome (GBS) have been reported in people who receive Td. GBS is a rare syndrome in which your body's immune system attacks your nervous system causing weakness and tingling in your extremities.

Saline Skin Prep:
Side effects that may be caused by the saline skin prep include:

- pain, tenderness, redness, hardness, itching, swelling, and/or warmth at the injection site
- cellulitis, an infection of the skin

Temozolomide:
The most common side effects of temozolomide are loss of appetite, nausea, constipation and decrease in blood cell counts. A decrease in the number of white blood cells may increase your risk of infections. A reduction in the number of platelets may increase the risk of bleeding and a reduced number of red blood cells may increase fatigue or shortness of breath. Some people who have taken temozolomide also had the following side effects:

- nausea and vomiting, especially on the first day of each cycle
- back, abdominal and/or stomach pain, breast pain
- diarrhea
- hair loss
- dry skin, skin redness, itching and/or rash
- swelling of extremities (your arms, legs, fingers, or toes)
- inflammation or swelling of the mouth, throat and/or sinuses
- headache, confusion, loss of memory, dizziness, fatigue, fever, and/or weakness
- anxiety, depression
- joint and muscle pain
- abnormal coordination when using your arms or legs (such as walking or feeding yourself) and/or abnormal feelings in your extremities
- trouble sleeping or sleepiness
- changes in your sense of taste
- changes in your vision such as double or blurred vision
- coughing or shortness of breath, respiratory tract infection
- urinary incontinence/frequency, urinary tract infection
- weight increase
- seizures, hemiparesis (weakness on one side of the body)
- adrenal hypercorticisim (elevated hormone levels)
- allergic reactions, sometimes severe
- hepatotoxicity (abnormal liver function tests); sometimes these may be severe, which is why liver function tests may be performed throughout temozolomide treatment cycles

Rarely, unusual ("opportunistic") infections have occurred. Rare cases of erythema multiforme (a skin condition that is similar to a bad rash) have been reported which got better after temozolomide was stopped and, in some cases, recurred upon restarting treatment with temozolomide.

Very rare side effects have included secondary cancers including leukemia and myelodysplastic syndrome (MDS). MDS is a disorder of the bone marrow in which blood cells that do not function normally are produced.

Reproductive studies have not been done with people who are taking temozolomide. Immature sperm and testicular atrophy occurred in studies with rats and dogs, using doses of temozolomide 1/4 and 5/8 of the recommended human doses. In animal studies, temozolomide caused death and multiple malformations in fetal rats and rabbits.

Leukapheresis:
Some side effects associated with the leukapheresis procedure may be similar to those experienced during blood donation and include light-headedness, fainting, vomiting, and rapid breathing. Other side effects which may occur that are unique to the leukapheresis procedure include chills caused by cooling of the blood when it is contained in the special machine, and tingling and nausea caused by low blood calcium

levels due to the blood thinner (called citrate) used to maintain free flow of the blood through the machine. These side effects can be controlled by altering the rate at which blood is withdrawn, by warm blankets, by altering the amount of blood thinner, by administration of calcium during the procedure, and by stopping the procedure.

Rarely, the leukapheresis procedure may be associated with loss of blood, breakdown of the blood, clotting of the blood, allergic reactions, inadvertent infusion of air, and fluid overload or depletion. These side effects can usually be controlled by stopping the procedure and providing appropriate medical care. In addition, there is always the risk that very uncommon or previously unknown side effects may occur or that life-threatening side effects may occur and death may result.

Central Venous Catheter Insertion for leukapheresis

If you require a special large intravenous (IV) line (called a "central venous catheter" or "catheter") for the leukapheresis procedure, a temporary catheter will be placed in a vein either in the neck (the jugular vein) or in the groin (the femoral vein). The doctor placing the catheter will describe the procedure and risks of the procedure and ask you to sign a separate consent form before the catheter placement. Numbing medication (xylocaine) will be given by a small injection into the skin at the site of central venous catheter placement. The catheter will be placed using ultrasound and live X-ray (fluoroscopy) for guidance. The catheter will be held in place by stiches in the skin, which may be removed once the catheter is firmly in place.

The risks of central catheter placement associated with this deeper venous catheter include:

- bruising around the catheter,
- injury to the vein or other blood vessels, nerves and/or organs close to the area of catheter placement,
- collapse of the lung, bleeding or fluid in the chest that could require chest tube placement,
- bleeding under the skin,
- infection,
- allergic reaction to local numbing medication,
- irregular heartbeat,
- clotting of the catheter or the blood vessel or irritation/redness of the vein.
- narrowing of the vein which may prevent future use of the vessel
- removal of the central venous catheter may cause discomfort, small amount of bleeding and pressure will need to be held in the area for 5-10 minutes (maybe longer).

There is also a very rare possibility that you may have symptoms ranging from dizziness and fainting to allergic reactions such as anaphylaxis.

This research study may require a central venous catheter for the leukapheresis procedure. The radiation you will receive from this procedure exposes a part of your body to a higher level of radiation than the rest of your body. The typical

radiation exposure from this procedure is about 200 μSv (20 millirem) which is equal to about 26 days of natural background radiation exposure.
If you have a central venous catheter inserted, you may need conscious sedation, which is a combination of medicines to help you relax and to block pain during the procedure. Conscious sedation lets you recover quickly and return to your everyday activities soon after your procedure. You will receive the medicine through an intravenous line (IV, in a vein). You may feel pain from the initial needle stick when placing the IV. Possible bruising from where the needle went into the skin may occur, as well as rarely, an allergic reaction to the medication. Vomiting or inhaling food contents from the stomach, feeling confused, low blood pressure, drowsiness, allergic reaction, vein irritation are also risks of sedation. These risks are minimized if you do not eat for a minimum of 6-8 hours prior to any procedure. You will sign a separate consent for this type of sedation.

MRI/MRS Imaging:
Magnetic resonance imaging (MRI) is a procedure that allows doctors to look inside the body by using a scanner that sends out a strong magnetic field and radio waves. This procedure is used routinely for medical care and is very safe for most people, but you will be monitored during the entire MRI scan in case any problems occur. The risks of MRI are:

The MRI scanner contains a very strong magnet. Therefore, you may not be able to have the MRI if you have any type of metal implanted in your body, for example, any pacing device (such as a heart pacer), any metal in your eyes, or certain types of heart valves or brain aneurysm clips. Someone will ask you questions about this before you have the MRI.

There is not much room inside the MRI scanner. You may be uncomfortable if you do not like to be in close spaces ("claustrophobia"). During the procedure, you will be able to talk with the MRI staff through a speaker system, and, in the event of an emergency, you can tell them to stop the scan. If have claustrophobia, you may require medication to help you relax ("sedation"). If you do require medication to relax, you should not drive a car, take part in activities like riding a bike, or perform other similar tasks until the next morning because the medication(s) can affect your thinking for several hours and can slow down your reflexes.

The MRI scanner produces a loud hammering noise, which has produced hearing loss in a very small number of patients. You will be given earplugs to reduce this risk.

If you are a woman of childbearing potential, there may be unknown risks to the fetus. Therefore, before you can have the MRI, you must have a pregnancy test.

Reproductive Risks:
Because the treatment in this study might affect an unborn baby, you should not become pregnant while on this study. Since this treatment will not be given to any patients who are pregnant, all women and adolescents of childbearing potential must take a pregnancy test prior to receiving any treatment on this study. We encourage all women and adolescents enrolled on this study to use one of the effective birth control

methods during treatment and for six months after treatment is stopped. These methods include total abstinence (no sexual intercourse), oral contraceptives ("the pill"), an intrauterine device (IUD), an etonogestrel implant (Implanon), or medroxyprogesterone acetate injections (Depo-Provera shots). If one of these cannot be used, using contraceptive foam and a condom are recommended. You must notify the doctor if you become pregnant during the course of this study.

You should not nurse a baby while receiving treatment on this study or for six months after completing treatment.

We do not know whether using this treatment will affect sperm. As a result, men and adolescents who have not had a vasectomy are advised to either (a) abstain from reproductive sexual intercourse or (b) use a condom and contraceptive foam during intercourse. These precautions should be taken while on therapy and for at least one month after completing therapy.

HIV Testing:
Testing positive for human viruses (HIV) can be upsetting. You will be provided with information on medical and support services that may be available to you. If you test positive for HIV and that information were to become public, you could have problems getting insurance or a job. Your identity and test results will be kept confidential to the extent permitted by Florida Law. If test results are released in accordance with Florida Law, this disclosure will be accompanied by the following statement: "This information has been disclosed to you from records whose confidentiality is protected by state law. State law prohibits you from making any further disclosure of such information without the specific written consent of the person to whom such information pertains, or as otherwise permitted by state law. A general authorization for the release of medical or other information is not sufficient for this purpose."

Blood Draws:
The risks of drawing blood from a vein include discomfort at the site of puncture; possible bruising and swelling around the puncture site; rarely an infection; and, uncommonly, faintness from the procedure.

Researchers will take appropriate steps to protect any information they collect about you. However, there is a slight risk that information about you could be revealed inappropriately or accidentally. Depending on the nature of the information, such a release of your information could upset or embarrass you, or possibly affect your insurability or employability. Questions 17-21 in this form discuss what information about you will be collected, used, protected, and shared.

This study may include risks that are unknown at this time.

Personal Information: Taking part in this research may involve providing information that you consider confidential or private. Efforts such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe. Researchers will take appropriate steps to protect any information they collect about you. However, there is a slight risk that information about you could be revealed inappropriately or

accidentally. Depending on the nature of the information, such a release could upset or embarrass you, or possibly affect your insurability or employability. Questions 13-17 in this form discuss what information about you will be collected, used, protected, and shared.

Participation in more than one research study or project may further increase the risks to you. If you are already enrolled in another research study, please inform one of the research team members listed in question 1 of the addendum or the person reviewing this consent with you before enrolling in this or any other research study or project. Throughout the study, the researchers will notify you of new information that may become available and might affect your decision to remain in the study. If you wish to discuss the information above or any discomforts you may experience, please ask questions now or call one of the research team members listed in question 1 of the addendum form.

If you wish to discuss the information above, please ask questions by email or call the study coordinator listed in question 1 of the addendum.

10a. What are the potential benefits to you for taking part in this research study?

It is entirely possible that you will not benefit from taking part in this study. However, it is hoped that the study vaccine may allow your immune system to better fight your tumor.

10b. How could others possibly benefit from this study?

Information gained from this study may help doctors advance the medical treatment for brain tumors.

11. What other choices do you have if you do not want to be in this study?

If you do not want to be in this study, treatment would include surgery, radiation therapy with temozolomide, and monthly cycles of temozolomide. You may also choose to participate in another research study, if one is available and you qualify, or you can choose to have no treatment.

Your participation in this study is voluntary and any decision to take part or not to participate in the study will in no way affect the quality of your care.

12a. Can you withdraw from this study?

You are free to withdraw your consent and to stop participating in this study at any time. If you do withdraw your consent, you will not be penalized in any way and you will not lose any benefits to which you are entitled.

If you decide to withdraw your consent to participate in this study for any reason, please contact one of the research team members listed in question 1 of the addendum.

If you have any questions regarding your rights as a research subject, please call the Institutional Review Board (IRB) office listed on the "Consent Addendum" attached.

12b. If you withdraw, can information about you still be used and/or collected?

If you withdraw from this study, no further information will be collected. Any information already collected during your participation may still be used.

12c. Can the Principal Investigator withdraw you from this study?

You may be withdrawn from the study without your consent for the following reasons:

- You are pregnant or become pregnant
- You are infected with HIV or hepatitis
- You did not receive enough temozolomide and/or radiation
- We are unable to make or give the study drug
- You do not follow the instructions given to you by the research staff
- You experience a side effect and your physician feels it would be in your best interest to stop study treatment
- The study is stopped

13. How will your health information be collected, used and shared?

If you agree to participate in this study, the Principal Investigator will create, collect, and use private information about you and your health. This information is called protected health information or PHI. In order to do this, the Principal Investigator needs your authorization The following section describes what PHI will be collected, used and shared, how it will be collected, used, and shared, who will collect, use or share it, who will have access to it, how it will be secured, and what your rights are to revoke this authorization.

Your protected health information may be collected, used, and shared with others to determine if you can participate in the study, and then as part of your participation in the study. This information can be gathered from you or your past, current or future health records, from procedures such as physical examinations, x-rays, blood or urine tests or from other procedures or tests. This information will be created by receiving study treatments or participating in study procedures, or from your study visits and telephone calls. More specifically, the following information may be collected, used, and shared with others:

- Information that identifies or could be used to identify you such as name, date of birth, address, telephone numbers, medical record number and exact dates collected from your past, current or future health records
- Complete past medical history
- Records of physical and neurological exams
- Laboratory, pathology, radiology, and other test results
- HIV and other infectious disease test results

- Records about medications and radiation therapy
- Ability or potential ability to conceive a child
- Records about side effects you may experience
- Information on how you are feeling that is collected during telephone calls

This information will be stored in locked filing cabinets or on computer servers with secure passwords, or encrypted electronic storage devices.

Some of the information collected may be sent to a Immunomic Therapeutics, Inc., a healthcare company developing vaccine technology, located in Rockville Maryland. If data is shared, it will be in the form of a limited data set, described below.

Some of the information collected could be included in a "limited data set" to be used for other research purposes. If so, the limited data set will only include information that does not directly identify you. For example, the limited data set cannot include your name, address, telephone number, social security number, photographs, or other codes that link you to the information in the limited data set. If limited data sets are created and used, agreements between the parties creating and receiving the limited data set are required in order to protect your identity and confidentiality and privacy.

14. For what study-related purposes will your protected health information be collected, used, and shared with others?

Your PHI may be collected, used, and shared with others to make sure you can participate in the research, through your participation in the research, and to evaluate the results of the research study. More specifically, your PHI may be collected, used, and shared with others for the following study-related purpose(s):

To find out if the investigational pp65 DC dendritic cell vaccine is effective for the treatment of glioblastoma when given with stronger doses of routine chemotherapy.

Once this information is collected, it becomes part of the research record for this study.

15. Who will be allowed to collect, use, and share your protected health information?

Only certain people have the legal right to collect, use and share your research records, and they will protect the privacy and security of these records to the extent the law allows. These people include:

- the study Principal Investigator (listed in question 1 of the addendum) and research staff associated with this project.
- other professionals at the institution where you are participating in this research study.
- the University of Florida Institutional Review Board which is responsible for the approval of this research study (IRB; an IRB is a group of people who are responsible for looking after the rights and welfare of people taking part in research)..

16. Once collected or used, who may your protected health information be shared with?

Your PHI may be shared with:

- the study sponsor (listed in Question 3 of this form).
- Your treating physician and other professionals involved in your care.
- The study's Data and Safety Monitoring Board, who is responsible for monitoring the safety of the participants.
- National Institutes of Health, National Cancer Institute, who previously funded this study.
- United States governmental agencies who are responsible for overseeing research, such as the Food and Drug Administration, the Department of Health and Human Services, and the Office of Human Research Protections .
- Government agencies who are responsible for overseeing public health concerns such as the Centers for Disease Control and federal, state and local health departments.
- Your insurance company for the purposes of obtaining payment.

Otherwise, your research records will not be released without your permission unless required by law or a court order. It is possible that once this information is shared with authorized persons, it could be shared by the persons or agencies who receive it and it would no longer be protected by the federal medical privacy law.

17. If you agree to take part in this research study, how long will your protected health information be used and shared with others?

Your PHI will be used and shared with others until the end of this study.

You are not required to sign this consent and authorization or allow researchers to collect, use and share your PHI. Your refusal to sign will not affect your treatment, payment, enrollment, or eligibility for any benefits outside this research study. However, you cannot participate in this research unless you allow the collection, use and sharing of your protected health information by signing this consent and authorization.

You have the right to review and copy your protected health information. However, we can make this available only after the study is finished.

You can revoke your authorization at any time before, during, or after your participation in this study. If you revoke it, no new information will be collected about you. However, information that was already collected may still be used and shared with others if the researchers have relied on it to complete the research. You can revoke your authorization by giving a written request with your signature on it to the Principal Investigator.

Since this research study is being conducted at several institutions, there is an Institution Specific "Addendum" to this consent form. Please read this addendum prior to agreeing to participate in this research study.

SIGNATURES

As an investigator or the investigator's representative, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this research study; the alternative to being in the study; and how the participant's protected health information will be collected, used, and shared with others:

_____ _____

Signature of Person Obtaining Consent and Authorization | Date

Consenting Adults. You have been informed about this study's purpose, procedures, possible benefits, and risks; the alternatives to being in the study; and how your protected health information will be collected, used and shared with others. You have received a copy of this Form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask other questions at any time.

Adult Consenting for Self. By signing this form, you voluntarily agree to participate in this study. You hereby authorize the collection, use and sharing of your protected health information as described above. By signing this form, you are not waiving any of your legal rights.

_____ _____

Signature of Adult Consenting & Authorizing for Self | Date

Parent/Adult Legally Representing the Subject. By signing this form, you voluntarily give your permission for the person named below to participate in this study. You hereby authorize the collection, use and sharing of protected health information for the person named below as described above. You are not waiving any legal rights for yourself or the person you are legally representing. After your signature, please print your name and your relationship to the subject.

_____ _____

Consent & Authorization Signature of Parent/Legal Representative | Date

_____ _____

Print: Name of Legal Representative | Print: Relationship to Participant:

_____

Print: Name of Subject

Participants Who Cannot Consent But Can Read and/or Understand about the Study. Although legally you cannot "consent" to be in this study, we need to know if you want to take part. If you decide to take part in this study, and your parent or the person legally responsible for you gives permission, you both need to sign. Your signing below means that you agree to take part (assent). The signature of your parent/legal representative above means he or she gives permission (consent) for you to take part.

_____ _____

Assent Signature of Participant Date