Official Title:

I-ATTAC: Improved Anti-Tumor Immunotherapy Targeted Against Cytomegalovirus in Patients With Newly-Diagnosed WHO Grade IV Unmethylated Glioma

NCT: NCT03927222

IRB Document Date: May 06, 2022

DUKE UNIVERSITY HEALTH SYSTEM

Consent To Participate In A Research Study
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IRB APPROVED
AS MODIFIED
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PROTOCOL NO.:	Pro00090683 WCG IRB Protocol #20190629 IRB00106436
SPONSOR:	Duke University Medical Center
INVESTIGATOR:	Mustafa Khasraw, MBChB, MD, FRCP, FRACP DUMC Box 3624 Durham, North Carolina 27710 United States
STUDY-RELATED PHONE NUMBER(S):	Mustafa Khasraw, MBChB, MD, FRCP, FRACP 919-684-5301 919-206-0493 (after hours)

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RESEARCH CONSENT SUMMARY

You are being asked for your consent to take part in a research study. This document provides a concise summary of this research. It describes the key information that we believe most people need to decide whether to take part in this research. Later sections of this document will provide all relevant details.

WHAT SHOULD I KNOW ABOUT THIS RESEARCH?

- Someone will explain this research to you.
- Taking part in this research is voluntary. Whether you take part is up to you.
- If you don't take part, it won't be held against you.
- You can take part now and later drop out, and it won't be held against you
- If you don't understand, ask questions.
- Ask all the questions you want before you decide.

HOW LONG WILL I BE IN THIS RESEARCH?

We expect that your taking part in this research will last 10 to 12 months, as long as your tumor has not grown back and will involve up to 10 study vaccine treatments.

WHY IS THIS RESEARCH BEING DONE?

The purpose of this research is to learn if an experimental vaccine called CMV pp65 DC can help to activate your immune system and help your body fight off the tumor cells in your brain. The safety of this treatment will also be studied.

WHAT HAPPENS TO ME IF I AGREE TO TAKE PART IN THIS RESEARCH?

If you decide to take part in this research study, the general procedures include a physical exam, medical history, vital signs, blood tests, and MRI scan of the brain to see if you are eligible to be in the study. You will need to undergo a procedure called a leukapheresis at the Duke University Medical Center Apheresis Unit. The first 3 CMV pp65 DC vaccines will be given over 6 weeks. You will return to clinic every 2 weeks to receive these vaccines.

After you have received your first three study vaccines, you will be asked to repeat the MRI of the brain and have another leukapheresis procedure. Vaccines will be given every 35 days for a total of 10 vaccine injections unless tumor progression occurs.

You will also be given Temozolomide or Temodar® (TMZ), which is an FDA-approved anti-cancer drug by your doctor as part of your standard care. You will receive only 1 cycle of TMZ meaning you will take TMZ daily for 21 days. This cycle will be completed before your first vaccine.

COULD BEING IN THIS RESEARCH HURT ME?

The most important risks or discomforts that you may expect from taking part in this research include:

- Injection of the study vaccine may cause an allergic reaction that can include redness or swelling at the injection site and itching.
- The leukapheresis procedure may be similar to risks experienced during blood donation and include discomfort or a swollen bruise at the site of needle puncture, a slight risk of developing a local infection at the site, and development of a small scar.
- The GM-CSF Injection may cause headache, bone pain, muscle and joint pains, fever, and chills.
- Temozolomide (TMZ) may cause loss of appetite, nausea and vomiting, especially on the first day of each cycle, constipation, and decrease in blood cell counts.

WILL BEING IN THIS RESEARCH BENEFIT ME?

The most important benefits that you may expect from taking part in this research is that this immunotherapy will allow your immune system to better fight your tumor. The knowledge gained from your participation may benefit others.

WHAT OTHER CHOICES DO I HAVE BESIDES TAKING PART IN THIS RESEARCH?

Instead of being in this research, your choices may include further surgery, chemotherapy and radiation.

WHAT ELSE SHOULD I KNOW ABOUT THIS RESEARCH?

For women, being a part of this study while pregnant may expose the unborn child to significant risks, some of which may be currently unforeseeable. You must agree to use 2 forms of appropriate contraceptive measures at the same time for the duration of the study vaccine administration and for 6 months afterwards.

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For men, participation in this research may damage your sperm, which could cause harm to a child that you may father while on this study. You must agree to use a medically acceptable form of birth control, in order to be in this study and for 6 months after the study vaccine administration.

DETAILED RESEARCH CONSENT

You are being asked to participate in a research study because you have a malignant brain tumor, which is usually treated with surgery, radiation, and chemotherapy.

Research studies are voluntary and include only people who choose to take part. Please read this consent form carefully and take your time making your decision. As the doctor or the study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. We encourage you to talk with your family and friends before you decide to take part in this research study. The nature of the study, risks, inconveniences, and discomforts, and other important information about the study are listed below.

Please tell your doctor or the medical staff if you are taking part in another research study.

A NIH grant will help sponsor this study. Portions of Dr. Mustafa Khasraw's and his research team's salaries will be paid by this grant. The CMV (cytomegalovirus) vaccine technology used in this study was developed by Drs. John Sampson, Gary Archer, and others at Duke and, if successful, both Duke and the developers could benefit financially. This technology, including the use of the tetanus-diphtheria (Td) vaccine, has been licensed to a Duke start-up company, Annias Immunotherapeutics. Duke University and Drs. Sampson and Archer have an equity interest (stocks and/or options) in the company.

WHO WILL BE MY DOCTOR ON THIS STUDY?

If you decide to participate, Dr. Mustafa Khasraw will be your doctor for the study; however, your treating neuro-oncologist will remain as your primary doctor for the treatment of your brain tumor and will be in contact with your regular health care provider throughout the time that you are in the study and afterwards, if needed.

WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to learn if a vaccine can help to activate your immune system and help your body fight off the tumor cells in your brain. The safety of this treatment will also be studied. The vaccine, called CMV pp65 DC, is investigational, which means that it is not approved by the US Food and Drug Administration (FDA) and is still being tested in research studies.

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It is believed that the body's immune (protection) system can attack tumor cells and kill them. This is thought to be due to immune cells called T-lymphocytes (T-cells), which can recognize special proteins on the surface of tumors as a signal to attack and fight the cancer. In most patients with advanced cancer, the immune system does not adequately destroy the tumor because the white blood cells or T-cells are not stimulated enough.

Before your T-cells can become active against tumor cells, they require strong stimulation. There are special "stimulator" cells in the body called Dendritic Cells (DCs) that can take up proteins released from cancer cells and present pieces of these proteins (called peptides) to T cells to create this strong stimulation. When the vaccine for this study is made, it will be "pulsed" or loaded with genetic material called RNA (ribonucleic acid), which stimulates the DC to change the RNA into a protein called pp65. This protein is produced by a common virus called Cytomegalovirus (CMV) that 70-80% of us have been exposed to in our lifetime. Recently, we have found that this virus is present in many malignant brain tumors. Brain tumors are very aggressive and, for reasons we do not yet understand, are difficult for the body to attack. The CMV virus is an area to target in the tumor that, if attacked by your immune systems cells, may prevent your tumor from growing.

It is hoped that, by injecting the CMV pp65 DC vaccine into your skin, your immune system will be activated against the protein. Once it is activated against this protein, your immune system may recognize this protein on the surface of the tumor cells and attack the tumor cells in your brain and not attack normal cells. Use of a vaccine that stimulates your immune system is called immunotherapy. An additional drug called granulocyte macrophage-colony stimulating factor (GM-CSF) will be mixed with the vaccine to help boost your immune system.

Tetanus-diphtheria (Td) immunization is a drug composed of deactivated (dead) tetanus and diphtheria toxins. It works by causing an immune response to produce antibodies, in order for the body to recognize antigens from tetanus and diphtheria toxins if they are ever introduced into the body. We have discovered through previous studies that giving the Td immunization prior to immunotherapy may help improve the effectiveness of the study drug by activating the immune response against antigens in the study drug vaccine.

Using Td in this way is considered investigational, since it has not been approved by the FDA for this use.

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HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Approximately 64 people will take part in this study at Duke.

WHAT HAS BEEN THE PRIOR EXPERIENCE WITH CMV PP65 DC IMMUNOTHERAPY?

Previous research studies using CMV pp65 DC vaccine have been conducted here at Duke for brain tumors. No serious side effects have been reported. In addition, patients have received DCs loaded with other substances at this and other institutions for the treatment of a variety of different tumors. Again, no serious side effects have been reported. The effectiveness of this type of therapy in treating tumors is unknown at the present time and is the reason for research studies such as this one.

WHAT IS INVOLVED IN THE STUDY?

If you agree to be in this study, you will be asked to sign this consent form. You have already undergone surgery to remove the brain tumor. In order for you to be eligible for this study, the surgery has to be very successful; almost the entire brain tumor needs to have been removed during surgery.

You will have the following tests and procedures to make sure that you are eligible:

- Physical exam and medical history
- Vital signs
- Blood tests
- MRI of the brain

We will need to review your pathology report from your brain tumor surgery to confirm that the brain tumor you have is a Grade IV glioblastoma. As part of further molecular diagnostic analysis of your tumor, slides from your surgery at Duke will be sent for standard biomarker analysis, which includes MGMT promotor methylation status and IDH-1/2 mutation analysis. If you have this surgery done at another hospital, different than Duke, and if such institutions do not incorporate these initial molecular diagnostic assays, slides from surgical blocks will be ordered for subsequent MGMT promoter methylation status and IDH-1/2 mutation analysis, so as to ensure the baseline molecular diagnostics of the tumor that was removed.

As an optional part of the study, we may sample a small amount of tissue from the original tumor that is removed and stored as a surgical specimen block at either Duke University or the external institution (depending on where the surgery was performed). This means obtaining histologic slides

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from the original specimen block stored at Duke or the external institution to perform detection of CMV in the tumor. Obtained slides will then be stored in the Duke Brain Tumor Immunotherapy Program (DBTIP) lab. The sampling of this tumor specimen will not exceed 10% of the original block so as to preserve adequate tissue should you or your doctor want future diagnostic testing as part of your clinical care or other clinical trials. This process is optional should you allow us to sample the tumor tissue.

Please **initial** next to one of the statements below to indicate whether or not you agree to allow the collection of slides from initial surgery specimen blocks for detection of CMV studies.

_____ **Initials** Yes, I agree to allow histologic slides to be obtained from the initial resection specimen for future research on CMV in tumor tissue.

_____ **Initials** No, I do not agree to allow histologic slides to be obtained from the initial resection specimen for future research on CMV in tumor tissue.

Leukapheresis: You will need to undergo a procedure called a leukapheresis at the Duke University Medical Center Apheresis Unit. Leukapheresis is a medical procedure by which large numbers of white blood cells can be removed from your circulation, however, it is not a standard procedure for brain tumor therapy. Leukapheresis requires the insertion of a needle into the veins of both arms, after which you lie on a bed for about 2-3 hours while blood is collected, much like in a standard blood donation. The main difference is that only the white blood cells are collected while the red blood cells are returned to your body. A portion of the removed white blood cells will be used to make the DCs for the vaccine. During leukapheresis, a medication called citrate is added to the blood while in the machine to keep the blood from clotting in the tubing. If you do not have sufficient venous access for the leukapheresis, a temporary intravenous catheter may need to be inserted in a deeper vein (central venous catheter).

If you underwent leukapheresis as part of another companion study titled "***Preliminary Testing and/or Procedures for Potential Clinical Trial Participants of the Preston Robert Tisch Brain Tumor Center,"*** the vaccines manufactured as part of that study will be used in the current study and any unused vaccine products will be handled as you indicated in the companion study.

Td: You will receive the standard dose of Td as an intramuscular injection in your arm before your first vaccine. It is thought that the Td immunization may help improve the effectiveness of the CMV

pp65 DC vaccine. In addition to receiving this Td booster immunization, you will receive Td mixed with saline (salt water) one day before your 4th CMV pp65 DC vaccine.

Initial CMV pp65 DC Vaccinations: The first 3 CMV pp65 DC vaccines will be given over the course of 6 weeks. You will return to clinic every 2 weeks to receive these vaccines. You will receive all vaccine injections with a thin needle that is about 1 ½ inches long, which will be placed just under the skin (intradermal) in the area below your groin in both the right and left side at each administration session. Each injection will only take a few seconds. After each vaccine, you will have vital signs taken. Because this is a study to assess the safety of this vaccine, it is possible you may receive a dose of the vaccine which only later demonstrated to be harmful. After you have received your first three study vaccines, you will be asked to repeat the MRI of the brain and have another leukapheresis procedure. The leukapheresis procedure will be to produce more DC vaccine for your continued vaccinations and to monitor the effect of the vaccine. It is possible that, if you continue to do well and your tumor does not come back, you may need to have an additional leukapheresis procedure to produce more DCs for more vaccines.

Chemotherapy Treatment: Temozolomide or Temodar® (TMZ) is an FDA-approved anti-cancer drug and will be given by your doctor as part of your standard care. You will receive only 1 cycle of TMZ, meaning you will take TMZ daily for 21 days. This cycle will be completed before your first vaccine. TMZ is a capsule that you take by mouth; the actual number of capsules you take will vary depending upon your height and weight. It should be taken in a fasting state (nothing to eat for one hour prior to each dose and for two hours after each dose). It has been well tolerated by both adults and children.

As part of your standard care at Duke, your tumor tissue will be tested for a biomarker that is referred to as O6-methylguanine-DNA methyltransferase (MGMT), if this test was not already performed on your tumor tissue. MGMT is a gene that has been shown to be important in predicting the response of glioblastoma to the chemotherapy drug temozolomide (TMZ). Tumors with unmethylated MGMT do not respond as well to TMZ as tumors with methylated MGMT. We will obtain the results of the MGMT test result from your medical record, and only individuals with unmethylated MGMT will be enrolled in this trial. Although individuals with unmethylated MGMT tumor appear to be less responsive to treatment with TMZ, there is a chance that treatment with TMZ could help shrink your tumor, and by signing this consent form you are choosing not to receive additional cycles of TMZ. There is a risk that the MGMT tumor testing may incorrectly identify your tumor type as unmethylated and result in you forgoing available therapy with TMZ.

Vaccinations: DC vaccines will be given every 35 days for a total of 10 vaccines unless tumor progression occurs.

During the study vaccine appointments, you will be checked for any side effects and/or symptoms. You will have your blood drawn to check your kidney function, your white blood cells, and your immune system. Approximately 6 tablespoons of blood will be drawn at the following time points: before the 1st leukapheresis, at the post radiation therapy/TMZ visit, on the day of but before the 1st and 3rd vaccines, on the day of but prior to pre-conditioning, before the 2nd leukapheresis, on same day of but before the 4th vaccine, and then prior to but on the same day as each remaining vaccine. If your tumor progresses, we would also like to draw approximately 6 tablespoons of blood at that time.

MRIs: You will also have several MRIs (magnetic resonance image) to confirm that the tumor is not growing. MRI is done initially to confirm you are eligible for this study, then every 2 months for the first year, after which you will have an MRI every 2 to 6 months at the discretion of your treating oncologist. To get better pictures with the MRI, we will inject a contrast agent into your veins when you get your MRI. MRI uses magnetic waves to make medical images of the body. MRI involves entering a large room in which a magnet is present. You will be placed on a narrow bed and then slid into a small tunnel approximately 6 feet in length and 25 inches in diameter. You will be asked to lie still for about one hour on this bed. You will hear a loud machine-like noise. You may be asked to have a harmless monitoring device applied during the study. During the study, you can have voice contact and physical contact with someone in attendance if you desire.

Follow-up Visits: After you complete the study vaccines, you will no longer be required to continue visits for this study, but you will continue to be examined periodically in accordance with routine care. An attempt will be made to obtain blood for immunologic monitoring 2-3 times a year at standard Duke neuro-oncology visits. We would like to repeat this blood draw for immunologic testing if you are told you have tumor progression. The study team may stay in contact with you through periodic phone calls to ask about your health and about any medications you have taken or are currently taking for the treatment of your tumor.

OPTIONAL STORAGE OF BLOOD AND TUMOR FOR FUTURE RESEARCH

As part of this study, you are also being asked to allow the study sponsor and PI to store your **unused** blood and tumor samples for future testing to learn more about how the study drug has worked and to further study the immunology of brain tumors. From these unused samples, it might

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also be possible to learn more about how to better treat your type of primary brain tumor, and for purposes that are not yet known.

The samples will be stored in the Duke Brain Tumor Immunotherapy Program (DBTIP) Laboratory where all other samples from this study are stored. The samples being stored are ONLY for this study. Our animal studies being done in the DBTIP Lab are identifying markers (like CMV) that may help the effectiveness of the study drug; therefore, as other markers are identified, we would like to investigate whether these same markers are found in your unused samples.

If you do not agree to banking of your unused samples, you can still take part in the main research study.

Withdrawing consent for the storage and future testing of your unused blood and tumor samples will result in destruction of the unused sample. However, if you withdraw your consent after the unused sample has been tested, the test results and the research study/sample-related information will remain in any database(s) that was created for the research study. The reason for this is to comply with regulations that require the sponsor to make data available for review by the FDA or other appropriate regulatory authorities, or if this research is used to support an application for FDA approval to market the study drug.

If you withdraw consent for participation in the main study or are discontinued from the main study, the unused blood and/or tumor samples you provided will continue to be available for storage and future testing unless you also withdraw your consent for this purpose as stated above. If you want to withdraw your permission for the storage of this blood and/or tumor for future testing, we ask that you contact Dr. Khasraw in writing and let him know you are withdrawing your permission for this unused portion of blood to be used for future research. His mailing address is: Dr. Mustafa Khasraw, The Preston Robert Tisch Brain Tumor Center, DUMC Box 3624, Durham, NC 27710.

Please **initial** next to one of the statements below to indicate whether or not you agree to allow storage of your unused samples for possible future research as part of this study in the Duke Brain Tumor Immunotherapy Program (DBTIP) Laboratory.

_____ **Initials** Yes, I agree to allow my unused blood and/or tumor samples to be stored for future research in the DBTIP Lab.

_____ **Initials** No, I do not agree to allow my unused blood and/or tumor samples to be stored for future research in the DBTIP Lab.

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WHAT IF MY TUMOR COMES BACK?

Your tumor may need to be biopsied or removed to confirm that the tumor has in fact come back as part of your routine clinical care outside of this research study. You will be asked to sign a surgical consent form if you have a biopsy or resection (removal of the tumor). If this is clinically indicated and performed here at Duke or an external institution, it is standard practice to contact you about consenting to provide tissue for research purposes. If you agree to participate in this study called the Duke Brain Tumor Center Biorepository study, you will sign a separate research consent and we will use a portion of tissue from that surgery specimen as part of this research study to see how well the immunotherapy worked in that tissue. This sampling includes obtaining slides sampled from the biopsy/resection specimen block to perform immunohistochemistry detection of CMV. Obtained slides will then be stored in the DBTIP lab. The sampling of biopsy/resection specimens will not exceed 10% of the specimen block so as to preserve adequate tissue should you or your doctor want future diagnostic testing as part of your clinical care or other clinical trials. You do not need to agree to participate in the Biorepository to be in this study.

Please **initial** next to one of the statements below to indicate whether or not you agree to allow the collection of slides from future biopsy/resection specimen blocks for detection of CMV studies.

_____ Yes, I agree to allow histologic slides to be obtained from a future biopsy/resection
Initials specimen for future research on CMV in tumor tissue.

_____ No, I do not agree to allow histologic slides to be obtained from a future
Initials biopsy/resection specimen for future research on CMV in tumor tissue.

HOW LONG WILL I BE IN THIS STUDY?

As long as the tumor has not grown back, you will receive the CMV pp65 DC vaccine monthly (following the first 3 bi-weekly vaccines) for a total of 10 vaccines (approximately 10 to 12 months from time of consent to vaccine #10). If an MRI suggests that the tumor has grown back, you will be offered other therapy and removed from the study.

After you complete the study vaccine treatments, we will continue to review your medical record for as long as you are followed at Duke and we may collect information about treatments you receive for your brain tumor. We may request your medical records when you are seen at another hospital, and we will contact your local physician's office to collect information about how you are doing. Whether or not your tumor progresses, we will continue to track the size of your tumor based on

MRI scans taken at Duke or elsewhere. The study team may continue to follow you through periodic phone calls to see how you are doing indefinitely.

You can choose to stop participating at any time without penalty or loss of any benefits to which you are entitled. However, if you decide to stop participating in the study, we encourage you to talk to your doctor first.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

Although we hope that this immunotherapy will allow your immune system to better fight your tumor, it is entirely possible that you will not benefit directly from this study. However, even if you do not benefit from the study directly, the knowledge gained as a result from your participation may benefit others.

WHAT ARE THE RISKS OF THE STUDY?

While in this study, you are at risk for possible side effects from the immunotherapy and the study procedures. You should discuss these with the study doctor. The known side effects are listed in this consent form, 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:

For those of Reproductive Potential

Female

Being a part of this study while pregnant may expose the unborn child to significant risks, some of which may be currently unforeseeable. Therefore, pregnant women will be excluded from the study. If you are a woman of childbearing potential, a blood pregnancy test will be done (using 1 teaspoon of blood drawn from a vein by needle-stick), and it must be negative before you can continue in this study. If sexually active, you must agree to use 2 forms of appropriate contraceptive measures at the same time for the duration of the study vaccine administration and for 6 months afterwards and for 6 months following bevacizumab administration, if applicable. Medically acceptable contraceptives include: (1) surgical sterilization (such as a tubal ligation or hysterectomy), (2) approved hormonal contraceptives (such as birth control pills, patches, implants or injections), (3) barrier methods (such as a condom or diaphragm) used with a spermicide, or (4) an intrauterine device (IUD). Contraceptive measures such as Plan B$^{(TM)}$, sold for emergency use after unprotected sex, are not

acceptable methods for routine use. If you do become pregnant during this study or if you have unprotected sex, you must inform your study physician immediately.

Male
Your participation in this research may damage your sperm, which could cause harm to a child that you may father while on this study. Such harm may be currently unforeseeable. If you are sexually active, you must agree to use a medically acceptable form of birth control for the duration of the study vaccine administration and for 6 months afterwards and for 6 months following bevacizumab administration, if applicable. Medically acceptable contraceptives include: (1) surgical sterilization (such as a vasectomy), or (2) a condom used with a spermicide. Contraceptive measures such as Plan B(TM), sold for emergency use after unprotected sex, are not acceptable methods for routine use. You should inform your partner of the potential for harm to an unborn child. She should know that if pregnancy occurs, you will need to report it to the study doctor, and she should promptly notify her doctor.

Td Vaccine (Adult Tetanus & Diphtheria)
With a vaccine, like any medicine, there is a chance of side effects. These are usually mild and go away on their own. Serious side effects are also possible, but are very rare. Most people who get Td vaccine do not have any problems with it.

Mild Problems Following Td
(Did not interfere with activities)
Most Likely
- Pain where the shot was given (about 8 people in 10)
- Redness or swelling where the shot was given (about 1 person in 3)

Likely
- Mild fever (about 1 person in 15)

Less Likely
- Headache or Tiredness (uncommon)

Moderate Problems Following Td
(Interfered with activities, but did not require medical attention)
- Fever over 102°F (rare)

Severe Problems Following Td
(Unable to perform usual activities; required medical attention)

- Swelling, severe pain, bleeding and/or redness in the arm where the shot was given (rare). Problems that could happen after **any** vaccine:
- Brief fainting spells can happen after any medical procedure, including vaccination. Sitting or lying down for about 15 minutes can help prevent fainting, and injuries caused by a fall. Tell your doctor if you feel dizzy, or have vision changes or ringing in the ears.
- Severe shoulder pain and reduced range of motion in the arm where a shot was given can happen, very rarely, after a vaccination.
- Severe allergic reactions from a vaccine are very rare, estimated at less than 1 in a million doses. If one were to occur, it would usually be within a few minutes to a few hours after the vaccination.

CMV pp65 DC Vaccine

Most likely

- Pain, redness, or swelling at the injection site

Less Likely

- Allergic reaction- The study vaccine may cause an allergic reaction. Symptoms of an allergic reaction may include:
    - itching
    - hives
    - low blood pressure
    - difficulty breathing
    - in rare occasions, death
- Swelling of the Brain (Cerebral Edema)- Cerebral Edema may be caused by the tumor, a dramatic increase in the number of immune cells in the brain, or the killing of tumor cells. Symptoms of swelling of the brain include:
    - severe headaches
    - confusion
    - lack of energy
    - unconsciousness
    - coma
    - losses of movement, sensation, or function in certain areas of the body

- In the event that you experience brain swelling after you receive DC vaccines due to an inflammatory response, your physician may treat you with a reduced dose of bevacizumab (also known by the brand name Avastin) for the swelling. The dose of bevacizumab you would receive is less than the full dose that is given to treat patients for a recurrence of their brain tumor. Bevacizumab will be administered through the vein approximately every three weeks, and the effects of the bevacizumab on the swelling will be evaluated by your physician after each MRI you receive. If your physician does not feel it is safe for you to receive bevacizumab, your physician may discuss other interventions with you, including steroids or surgery, to treat the inflammatory response to DC vaccination.
- Delayed Autoimmune Disease- The CMV pp65 DC vaccine 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, although this is very unlikely this type of severe reaction can cause serious injury or death.
- Infection- There may be a small risk of infection due to potential contamination of the injection during the manufacturing or mixing process. This may result in redness, swelling, and/or irritation at the injection site, and in extremely rare cases, a severe blood infection that could lead to death.

There may also be risks with the use of this study drug with the standard of care medications and procedures that you will receive such as the chemotherapy that are not known.

It is possible that additional side effects not previously seen or predicted may occur with the combination of the CMV pp65 DC vaccine and Td toxoid; these may be mild or very serious. Please immediately tell the study doctor or study staff if you have any side effects or problems during the study.

Sargramostim (GM-CSF)
The GM-CSF Injection may cause some, all, or none of the side effects listed below:

More likely
- Headache
- Bone pain
- Muscle and joint pains
- Fever and chills
- Rash and itchiness
- A feeling of discomfort or not feeling well and/or tiredness

Likely

- Stomach or abdominal pain or cramps
- Weakness
- Loss of appetite
- Nausea and/or vomiting
- Diarrhea
- Excessive sweating
- Inflammation of a vein through which the vaccine was given
- Redness and pain at the injection site
- Weight gain
- Fewer platelets in the blood. A low number of platelets may cause you to bruise and bleed more easily.
- Increase in the blood of certain enzymes or bilirubin (a substance that comes from the liver where waste products are broken down), which could indicate liver irritation or damage
- Elevation in the blood of creatinine, which normally is removed from the blood by the kidney and could indicate kidney damage
- Fluid build-up in the tissues usually of the lower legs

Less Likely

- Severe allergic reaction, which can be life threatening with shortness of breath, low blood pressure, and a rapid heartbeat
- A severe reaction, which can cause shortness of breath, a low blood pressure, a rapid heart rate, fever, a feeling of warmth and back pain and which may occur only with the first dose, but not with further doses
- An abnormally rapid heartbeat
- Leakage of fluid into the lungs which may result in shortness of breath and difficulty breathing and/or leakage of fluid into body tissues with puffiness of legs, arms or abdomen, weight gain and a drop in blood pressure
- Inflammation of the lungs, which may lead to pain and shortness of breath
- A build-up of fluid around the heart, which may be painful

Temozolomide

Most Likely

- loss of appetite
- nausea and vomiting, especially on the first day of each cycle
- constipation
- 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:

Likely

- back, abdominal and/or stomach pain, breast pain
- diarrhea
- hair loss
- dry skin, skin redness, itching and/or rash
- swelling of extremities
- inflammation 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, gait and/or feelings in extremities
- trouble sleeping or sleepiness
- change in sense of taste
- visual changes 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 reaction, sometimes severe

Less Likely

- Rarely, unusual ("opportunistic") infections have occurred. Rare cases of erythema multiforme (skin condition) have been reported which resolved after discontinuation of temozolomide and, in some cases, recurred upon restarting treatment with temozolomide. Another, rare yet serious side effect is liver damage which may cause yellowing of eyes and skin, swelling and may result in liver failure.
- 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 temozolomide. Immature sperm and testicular atrophy occurred in studies with rats and dogs, using doses of temozolomide ¼ and 5/8 of the recommended human doses. In animal studies, temozolomide caused death and multiple malformations in fetal rats and rabbits exposed during pregnancy.

If applicable, risks of bevacizumab (a drug often used for the management of malignant glioma that blocks blood vessel growth; blood vessels "feeding" the tumor are required for the tumor to grow) include: (Note: The risks below are for the standard dose of bevacizumab used to treat recurrent malignant glioma. If your study doctor feels you require bevacizumab, you will receive a dose in the study that is half the standard dose.)

Very Common (20% or more of patients)

- High blood pressure (hypertension), which may cause headache or blurred vision
- Abdominal Pain

Common (4-20% of patients)

- Numbness, tingling or pain in the fingers or toes (peripheral sensory neuropathy)
- Low numbers of white blood cells (neutropenia, leucopenia and lymphopenia) potentially associated with fever. Low white cell count may increase the risk of infection.
- Low numbers of platelets (thrombocytopenia)
- Shortness of breath (dyspnea)
- Diarrhea
- Bleeding from the rectum (rectal hemorrhage)
- Nausea and vomiting
- Pain, including headache and joints pain (arthralgia)

- Alteration in speech (dysarthria)
- Constipation
- Mucosal inflammation or inflammation of the mouth (stomatitis)
- Protein in the urine
- Mucocutaneous bleeding, including nose bleed (epistaxis)
- Lack of energy, weakness (asthenia, fatigue), or dizziness
- Loss of appetite (anorexia), or heartburn
- Body water loss (dehydration)
- Fever (pyrexia)
- Runny nose (rhinitis), stuffy nose, hoarseness, or cough
- Dry skin, flaking and inflammation of the skin (exfoliative dermatitis), change in skin color (skin discoloration)
- Change in the sense of taste (dysgeusia)
- Problems with the eyes (eye disorder), tearing (lacrimation increased)
- Low numbers of red blood cells (anemia) which may require blood transfusion
- Abnormal heartbeat which may cause palpitations or fainting
- Internal bleeding which may cause black tarry stool, vomit in blood, coughing up blood, or blood in urine
- Delay in healing of wounds or spontaneous opening of wounds. Fatal outcomes have been reported.
- Damage to jawbone which may cause loss of teeth
- Allergic reaction during or after infusion of bevacizumab which may cause fever, chills, rash, itching, hives, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Blood clot in limbs or lungs which may cause swelling, pain or shortness of breath
- Infection, presence of bacteria in the blood (sepsis), collection of pus in tissue or organs (abscess)

Occasional (3% or less of patients)

- A tear or a hole in the gut (perforation of the gastrointestinal tract)
- Abnormal tube-like connection (fistula) between internal organs such as the nose, throat, lungs, esophagus, rectum or vagina that are not normally connected. These conditions may cause serious infections or bleeding and require surgery to repair.
- Bleeding (hemorrhage), including bleeding associated with the tumor
- Clogging of a vessel in the lung (pulmonary embolism)

- Blocking of the arteries by a blood clot, including stroke (cerebral vascular accident) or heart attack. This risk is significantly increased in patients who are elderly or with a history of diabetes.
- Heart failure (cardiac failure congestive), especially in patients who have taken certain chemotherapy treatments in the past (doxorubicin or mitoxantrone) and rapid beating of the heart (supraventricular tachycardia)
- Rapid beating of the heart (supraventricular tachycardia)
- Blood clots in the veins (deep vein thrombosis)
- Abdominal pain
- Blockage in the intestine (ileus, intestinal obstruction)
- Pain, tenderness, or blistering on the fingers or feet (hand-foot syndrome, palmar-plantar erythrodysesthesia syndrome)
- Reduced consciousness, sleepiness, feeling tired (somnolence, lethargy)
- Low levels of oxygen in the blood (hypoxia)
- Fainting (syncope)
- Gastrointestinal disorder
- Voice changes, hoarseness (dysphonia)
- Muscular pain (myalgia) and muscular weakness
- Flesh-eating bacteria syndrome, an infection in the deep layers of the skin
- Kidney damage which may require dialysis

Uncommon (0.1% to Less than 1% of patients)

- Abnormal connection between the windpipe (trachea) and the esophagus (the tube that connects the mouth to the stomach) (tracheo-esophageal fistula)
- A hole in the gut lining of the stomach or duodenum (gastro-intestinal ulcer)

Rare (0.01% to Less than 0.1% of patients)

- Reversible posterior leukoencephalopathy syndrome: this may include symptoms of impaired brain function (headaches, vision changes, confusion, or seizures), and often, high blood pressure

Very Rare (Less than 0.01% of patients)

- Hypertensive encephalopathy: this may include symptoms of impaired brain function (headaches, vision changes, confusion, or seizures), and often, high blood pressure

Frequency Unknown

- Lesion in the gums with an exposed jawbone that does not heal and may be associated with pain and inflammation of the surrounding tissue (osteonecrosis of the jaw) in particular when treated with "bisphosphonate drugs" in this trial or in the recent past.
- A hole in the gallbladder (gallbladder perforation)
- A hole in the nasal passage (nasal septum perforation)
- Abnormalities to the fetus/unborn child when bevacizumab is given during pregnancy

In trials for colorectal cancer using bevacizumab and chemotherapy, female subjects had a 32% higher incidence of ovarian failure with early menopause (loss of menstrual cycle) and sterility (inability to have children) than subjects using chemotherapy alone.

Blood Draws: Blood draws (venipuncture) are the taking of blood from a vein in your arm by needle stick. The risks associated with drawing blood from your arm include momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or fainting is also possible, although unlikely.

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

As mentioned above, each of the MRIs will be conducted with a contrast agent to better see if any tumor is present. Contrast is given routinely to obtain better MRI scans of the brain. It is administered through a catheter placed in your vein. The catheter placement is similar to drawing blood except that the catheter remains in the vein during the time the contrast agent is being delivered. The risks of a blood draw and insertion of a catheter are similar. There have been a few,

rare cases of allergies to the agent used in MRI contrast enhanced scans. Subjects with allergies (such as rash) may be given Tylenol (acetaminophen) and Benadryl (diphenhydramine) prior to injection of the contrast.

A rare but serious adverse reaction has been observed in patients that received a gadolinium-based contrast material during MRI examinations, a reaction called nephrogenic systemic fibrosis (NSF). Patients with kidney disease are at increased risk of developing NSF. NSF may cause skin thickening, joint pain and/or swelling. In rare cases, NSF can lead to lung and heart problems and cause death. To minimize the likelihood that you will be affected, you will have a blood test to measure your kidney function. If your blood test is abnormal, you will not be permitted to receive gadolinium.

Leukapheresis: Some side effects associated with the leukapheresis procedure may be similar to those experienced during blood donation and include discomfort or a swollen bruise at the site of needle puncture, a slight risk of developing a local infection at the site, and development of a small scar. In addition, there can be light-headedness, fainting, vomiting, and rapid breathing. Some side effects that may occur are unique to the leukapheresis procedure and include chills caused by cooling of the blood when it is contained in the special machine, as well as tingling and nausea caused by the blood thinning medicine (citrate) that prevents the blood from clotting while in transit within the machine or its tubing. These side effects can be controlled by slowing the rate at which blood is withdrawn, by warm blankets, by changing the amount of the blood thinning medicine, by giving calcium supplements (tablets taken by mouth or liquid administered by vein), or by discontinuing the procedure. Rarely, the leukapheresis procedure may be associated with loss of blood, breakdown of the blood, clotting of the blood, allergic reactions, accidental addition of air to the blood going back to you, and fluid overload resulting in shortness of breath or fluid loss resulting in decreased blood pressure. If you require a central venous catheter for the leukapheresis procedure, the risks associated with this deeper venous catheter are air in the chest (~6%) due to a punctured lung, bleeding or fluid in the chest (~2%), and bleeding under the skin (~0.3%) and infection (~3%). However, procedures have been developed that use ultrasound (US) devices and fluoroscopy to provide imaging of the central veins during catheter placement. The advantages associated with using US and fluoroscopy include detection of exact vessel location, avoiding veins with clots, and guiding the proper placement of the catheter. Only personnel trained in the use of US and fluoroscopy central line placement at Duke will perform these procedures. These procedures involve a small amount of radiation. The radiation exposure from this procedure is about 200 microsievert.

The side effects listed for leukapheresis can usually be controlled and treated by discontinuing the leukapheresis procedure and by providing appropriate and immediate 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.

Other Risks: Subclinical (no signs or symptoms) autoimmunity may occur, although it is extremely unlikely. This could be secondary to the disease process itself, the surgical procedure, radiation, CMV pp65 DC vaccine, Td toxoid, chemotherapy, the immune response in the brain, or the destruction of tumor cells. Symptoms vary according to the particular disorder and are many; however, some of the symptoms could include depression, fatigue, itching/rash, nausea and/or vomiting, diarrhea, cramping, eye irritation/pain/redness/swelling, or various symptoms from pituitary gland disturbances. You will be monitored throughout the course of the study for any of these symptoms. Symptoms that fail to respond to medical therapy may lead to permanent impairment or even death.

Drug and Food Interactions: For your safety, you must tell the study doctor or study nurse about all the prescribed medical foods and drugs, herbal products, over-the-counter (OTC) drugs, vitamins, natural remedies and alcohol that you are taking before you start the study and before taking any of these products while you are on the study.

Due to the possible interference by antihistamines (such as Benadryl, Zyrtec, etc.), you are requested to avoid taking any antihistamines 2 days before, on the day of the vaccine administration, and for 2 days following the vaccine administration. If you have a condition or allergy that requires that you continue using antihistamines, please alert the study team. Dr. Khasraw and your doctors will decide if it is safe for you to hold the medication during vaccine administrations.

There may be risks, discomforts, drug interactions or side effects that are not yet known.

WHAT ALTERNATIVES ARE THERE TO PARTICIPATION IN THIS STUDY?

Your decision to receive this vaccine study drug is completely voluntary. You do not have to receive the CMV pp65 DC vaccine if you don't want to, and you can change your mind at any time. There will be no penalty to you, and you won't lose any benefits to which you are otherwise entitled. Your regular medical care will not change if you decide not to receive the CMV pp65 DC vaccine. If you want to stop receiving the vaccine, please tell your study doctor.

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Alternative treatments for your cancer could include further surgery, chemotherapy, radiation, or participation in a different research study protocol. You can also elect to have treatment of your symptoms only. This is frequently referred to as comfort care. Comfort care includes pain medication and other support. It aims to maintain your comfort and dignity rather than cure disease. Usually this care can be provided at home.

Please discuss all of your choices with the study doctor.

WILL MY INFORMATION BE KEPT CONFIDENTIAL?

Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total confidentiality. Your personal information may be viewed by individuals involved in this research and may be seen by people including those collaborating, funding, and regulating the study. We will share only the minimum necessary information in order to conduct the research. Your personal information may also be given out if required by law. Any human samples received and stored by the DBTIP will be assigned an All Laboratory Processed Specimen (ALPS) number (a unique number assigned only to samples) and will also include the assigned study number, type of sample, and date received. No stored samples have subject initials.

Your study records will be kept in a secure area and only authorized personnel will have access. As part of the study, Dr. Mustafa Khasraw and his study team will have access to the study results and will report the results and dates of your study-related tests and procedures to those named below. Some of these tests and procedures would have been done as part of your regular care. The PI will use these test results both to treat you and to complete this research. These test results will be recorded in your medical record and will be reported to the Department of Neurosurgery at Duke University Health System. Results of tests and studies done solely for this research study and not as part of your regular care will also be included in your medical record. As a participant of this study, you have the right to access your personal health information at any time.

Your records may be reviewed in order to meet federal or state regulations. Reviewers may include representatives from the Food and Drug Administration, the National Institute of Health, the National Cancer Institute, the Department of Neurosurgery at Duke, the Duke University Health System Institutional Review Board, the Duke Office of Audit, Risk and Compliance, the Duke Cancer Institute, the Institutional Review Board (IRB), Annias Immunotherapeutics, Inc., and others as appropriate. If your records are reviewed by any of these groups, they may also need to review

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your entire medical record. If this information is disclosed to outside reviewers for audit purposes, it may be further disclosed by them and may not be covered by the federal privacy regulations.

The study results will be retained in your research record for at least six years after the study is completed. At that time, either the research information not already in your medical record may be destroyed or information identifying you will be removed from the study results at Duke University Health System. Any research information in your medical record will be kept indefinitely.

Your study data will be provided to Annias Immunotherapeutics, Inc.; however, your identity will not be revealed.

While the information and data resulting from this study may be presented at scientific meetings or published in a scientific journal, your name or other personal information will not be revealed.

You will be told of any significant new findings developed during the course of this study that may relate to your willingness to continue your participation.

Some information collected about you only for this research study may be kept in a research study record separate from your medical record, and some research information may also be part of your medical record. You will not have access to this research information until the end of the study. However, it will be available to your physicians if needed for your care.

Some people or groups who receive your health information might not have to follow the same privacy rules. Once your information is shared outside of DUHS, we cannot guarantee that it will remain private. If you decide to share private information with anyone not involved in the study, the federal law designed to protect your health information privacy may no longer apply to the information you have shared. Other laws may or may not protect sharing of private health information.

The Department of Health and Human Services (DHHS) has issued a Certificate of Confidentiality to further protect your privacy. With this Certificate, the investigators cannot be forced (for example by court subpoena) to disclose research information that may identify you in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings. Disclosure will be necessary, however, upon request of DHHS for audit or program evaluation purposes.

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You should understand that a Confidentiality Certificate does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. Note however, that if an insurer or employer learns about your participation, and obtains your consent to receive research information, then the investigator may not use the Certificate of Confidentiality to withhold this information. This means that you and your family must also actively protect your own privacy.

Finally, you should understand that the investigator is not prevented from taking steps, including reporting to authorities, to prevent serious harm to yourself or others.

WHAT ARE THE COSTS?

You or your insurance provider will be responsible and billed for all costs related to your routine medical care, including copayments and deductibles. Routine medical care services are those that you would have received for your condition if you were not participating in this research study. Not all services are covered by insurance. Some procedures or scans may require pre-authorization by your insurance plan. We will notify you if we learn that a service is not covered by your insurance plan as part of the pre-authorization process. If it is not covered, you will be responsible for paying for it. The amount of your out-of-pocket expense will depend on your insurance plan. For beneficiaries with Medicare Advantage Plans, traditional Medicare is billed for the routine cost of a research study. You may have more or higher co-pays than with a Medicare Advantage plan. Please discuss the costs of the study with your study doctor**.** At your request, a Financial Counselor in the clinic may provide you with an estimate of costs for routine services.

Taking part in this study may cost you and/or your insurance company more than the cost of getting regular medical treatment.

Please talk with the study team about the specific services and procedures that the sponsor will pay for, and the ones for which you or your insurance will be responsible. We will monitor your DUHS patient care charges to make sure that costs are directed appropriately. If you have any questions or concerns about appropriate billing, contact your study team coordinator so that he/she can help find a resolution.

Duke will provide the pp65 CMV DC vaccines free of charge to you while you are taking part in the study. Other research-related costs that will be provided free of charge to you while you are taking

part in the study are listed below. The following are research-related costs that will not be charged to you or your insurance:

- Leukapheresis
- Td vaccine (Adult Tetanus & Diphtheria) used in preconditioning
- DC vaccines
- Immunologic testing on your blood samples

WHAT ABOUT COMPENSATION?

You will receive no compensation for participating in this study. There are also no plans to provide any compensation to you for any new products or discoveries that may result from your participation in this research or from the use of your blood or tumor samples.

WHAT ABOUT RESEARCH RELATED INJURIES?

Immediate necessary medical care is available at Duke University Medical Center in the event that you are injured as a result of your participation in this research study. However, there is no commitment by Duke University, Duke University Health System, Inc., or your Duke physicians to provide monetary compensation or free medical care to you in the event of a study-related injury.

For questions about the study or research-related injury, contact Dr. Khasraw at 919-684-5301 during regular business hours and at 919-206-0493 after hours and on weekends and holidays.

WHAT ABOUT MY RIGHTS TO DECLINE PARTICIPATION OR WITHDRAW FROM THE STUDY?

You may choose not to be in the study, or, if you agree to be in the study, you may withdraw from the study at any time. If you withdraw from the study, no new data about you will be collected for study purposes unless the data concern an adverse event (a bad effect) related to the study. If such an adverse event occurs, we may need to review your entire medical record.

Your decision not to participate or to withdraw from the study will not involve any penalty or loss of benefits to which you are entitled, and will not affect your access to health care at Duke. If you do decide to withdraw, we ask that you contact Dr. Mustafa Khasraw in writing and let him know that you are withdrawing from the study. His mailing address is: Dr. Mustafa Khasraw, The Preston Robert Tisch Brain Tumor Center, DUMC 3624, Durham, N.C. 27710. Dr. Khasraw may ask you to return for a check-up before you stop your study vaccinations if he thinks that stopping the vaccination suddenly may harm you. He may also ask you to complete the tests that would ordinarily occur when a person completes the study.

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We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

Your doctor may decide to take you off this study if your condition gets worse, if you have serious side effects, or if your study doctor determines that it is no longer in your best interest to continue. The sponsor or regulatory agencies may stop this study at any time without your consent. Reasons why this might occur include: if you need additional medication, don't follow the study plan, experience a study-related injury, or for administrative reasons. If this occurs, you will be notified and your study doctor will discuss other options with you.

Your samples and/or data may be stored and shared for future research without additional informed consent if identifiable private information, such as your name and medical record number, are removed. If your identifying information is removed from your samples or data, we will no longer be able to identify and destroy them.

Please **initial** next to one of the statements below to indicate whether or not you agree to allow your samples and/or data to be stored and shared for future research without additional informed consent if identifiably private information is removed.

_____ **Initials** Yes, I agree to allow my samples and/or data to be stored and shared for future research without additional informed consent if identifiably private information is removed.

_____ **Initials** No, I do not agree to allow my samples and/or data to be stored and shared for future research without additional informed consent if identifiably private information is removed.

If you agree to allow your tissue/blood/cells to be kept for future research with identifying information that could link your sample to you, you are free to change your mind at any time. We ask that you contact Dr. Khasraw in writing and let him know you are withdrawing your permission for your identifiable tissue/blood/cells to be used for future research. His mailing address is Dr. Mustafa Khasraw, The Preston Robert Tisch Brain Tumor Center, DUMC 3624, Durham, N.C. 27710. At that time, we will ask you to indicate in writing if you want the unused identifiable tissue/blood/cells destroyed or if your samples (having all identifying information removed that would link the sample to you) could be used for other research.

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The use of your data and samples may result in commercial profit. You will not be compensated for the use of your data and samples other than what is described in this consent form.

A description of this clinical trial will be available on https://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or a research-related injury, or if you have problems, concerns, questions, complaints or suggestions about the research, contact Dr. Khasraw at 919-684-5301 during regular business hours and at 919-206-0493 after hours and on weekends and holidays.

For questions about your rights as a research participant, or to discuss problems, concerns or suggestions related to the research, or to obtain information or offer input about the research, contact:

WCG Institutional Review Board (WCG IRB)
1019 39th Avenue SE Suite 120
Puyallup, Washington 98374-2115
Telephone: 855-818-2289 or 360-252-2500
E-mail: researchquestions@wcgirb.com

WCG IRB is a group of people who perform independent review of research.

WCG IRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WCG IRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

You may also contact the Duke University Health System Institutional Review Board (IRB) Office at (919) 668-5111.

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STATEMENT OF CONSENT

"The purpose of this study, procedures to be followed, risks and benefits have been explained to me. I have been allowed to ask questions, and my questions have been answered to my satisfaction. I have been told whom to contact if I have questions, to discuss problems, concerns, or suggestions related to the research, or to obtain information or offer input about the research. I have read this consent form and agree to be in this study, with the understanding that I may withdraw at any time. I have been told that I will be given a signed and dated copy of this consent form."

Signature of Subject	Date	Time
Signature of Person Obtaining Consent	Date	Time