EMORY | WINSHIP CANCER INSTITUTE
A Cancer Center Designated by the National Cancer Institute

You Are Being Asked to Be in a Research Study
Concise presentation of key concepts

You are being asked to be in a research study. A research study is designed to answer a scientific question. If you agree to be in the study you will be one of 5 people who are being studied, at Emory.

Why is this study being done?

This study is being done to answer the question: is the study drug, nivolumab, effective on the brain's immune system in people who have had a return of glioblastoma brain tumors? You are being asked to be in this research study because you have glioblastoma brain tumor.

Do you have to be in the study?

It is your decision to be part of this research study. You do not have to be in it. Your choice will not affect your access to medical care for your condition. Before you make your decision, you should take time to learn about the study.

What do I have to do if I choose to participate in this study?

If you are eligible and want to be part of the study, you will participate for until/unless your tumor comes back. The researchers will ask you to do the following: review medical history, physical examination, blood tests, urinalysis, electrocardiogram (ECG), chest x-ray, MRI scan, and hospitalization due to surgery. Some of these procedures will be paid for by the study.

How is this study going to help you?

If you are in the study, you will be helping the researchers answer the study question.

What are the risks or discomforts I should know about before making a decision?

The study will take time. The drug that is being tested may not work any better than regular care, and may even cause harm. All studies have some risks. Some risks are relatively small, like being bored or losing time. Some are more serious – for this study, these include risks of the drug, some of which include, lymph node inflammation, diabetes, blockage of bile ducts, irregular heart beat, fluid in the lungs,

loss of privacy, and breach of confidentiality. A full list of expected risks, their frequency and severity are in the "What are the possible risks and discomforts?" section of this document.

Alternatives to Joining This Study
The alternative to being in this study is to receive medical or surgical treatment for your GBM at Emory or elsewhere. Medical care for GBM that has regrown may include radiation, chemotherapy and/or surgery.

Costs
The study will pay for some of the items and procedures in this study. It will not pay for your regular medical care. More information is below in the Costs section of the consent form.

What Should I Do Next?
Read this form, or have it read to you. Make sure the study doctor or study staff explains the study to you. Ask questions (e.g., about exact time commitment, about unfamiliar words, more details on specific procedures, etc.) Make sure you understand which parts of these are research and which are standard care that you would have even if you did not join the study. Take time to consider this, and talk about it with your family and friends.

Emory University
Consent to be a Research Subject / HIPAA Authorization

Title: 18-N-0077: Cytokine microdialysis for real time immune monitoring in glioblastoma patients undergoing checkpoint blockade

IRB #: STUDY00001398

Principal Investigator: Edjah Nduom, MD

Sponsor: National Institute of Neurological Disorders and Stroke (NINDS)

Study-Supporter: Bristol-Myers Squibb

Introduction

You are being asked to be in a medical research study. This form is designed to tell you everything you need to think about before you decide if you want to be a part of the study. **It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study.** The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.

Before making your decision:

- Please carefully read this form or have it read to you
- Please listen to the study doctor or study staff explain the study to you
- Please ask questions about anything that is not clear

You can take a copy of this consent form, to keep. Feel free to take your time thinking about whether you would like to participate. You may wish to discuss your decision with family or friends. Do not sign this consent form unless you have had a chance to ask questions and get answers that make sense to you. By signing this form you will not give up any legal rights.

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

What is the purpose of this study?

The purpose of this study is to look at the effects of a drug, nivolumab, on the brain's immune system in people who have had a return of glioblastoma brain tumors. We will also look at the effects of nivolumab and an experimental drug, BMS-986016, on the brain tumor.

Background

Glioblastoma (GBM) brain tumors almost always return after treatment with surgery, radiation or drugs. When a GBM tumor returns, people usually have more surgery to remove as much of the tumor as possible. The tumor can never completely be removed by surgery, so most people also receive drugs, like chemotherapy. Many types of cancer are use drugs that help the body's own immune system attack tumors. Nivolumab is an immunotherapy drug that is used to treat some types of cancer such as lung cancer or melanoma. Recent studies in GBM suggest that nivolumab alone

does not treat returned GBM. Therefore, in this study, we will combine nivolumab with an experimental drug called BMS-986016. BMS-986016 also works on the immune system. We will see if BMS-986016 is safe to combine with nivolumab. We will see how the 2 drugs together affect returned GBM tumors.

We will also study the effects of nivolumab on the brain's immune system and on genes involved in the immune system. We will use small tubes, called microdialysis catheters, put into the brain to collect brain fluids and molecules. We will look at immune cells and genes before and after the first dose of nivolumab. The microdialysis catheters we will use are not FDA approved and are also experimental. These tubes are very similar to microdialysis catheters used in people who have had brain injuries.

What will I be asked to do?

Study Overview
This study requires an initial visit lasting 1-2 days to see if you are eligible to participate. If you are eligible, you will be hospitalized for 2 weeks. During the hospitalization you will have 2 surgeries. During the first surgery we will take a sample of the tumor and place the microdialysis tubes, as described below. The second surgery, one week later, will be to remove the tubes and as much of the tumor as possible. After leaving the hospital, you will have outpatient visits lasting about 5 hours every other week until there are signs that the tumor has returned.

The first surgery is for research purposes only. During the first surgery, we will take a tissue sample of your tumor. We will place two experimental tubes into the brain. One tube will go into the tumor. One tube will go into the brain around the tumor. We will do 2 other procedures during the first surgery. We will place a third small tube into your back, between the bones of the spine and into the fluid-filled sac surrounding the spinal cord. We will use that tube to collect spinal fluid over the next week. All of the surgery procedures will be done while you are under general anesthesia.

After surgery, you will be monitored in the intensive care unit. Two days after the surgery, you will receive a single dose of nivolumab. Cerebrospinal fluid (CSF) samples will be taken periodically throughout the next week from the tubes in the brain and your back. We will also draw blood samples.

Seven days after your first surgery, you will have the second surgery. During the second surgery, we will remove as much of your tumor as safely possible. We will remove the tubes in your brain and back. All of these procedures will be done while you are under general anesthesia.

Sixteen days after the surgery, you will start getting nivolumab and BMS-986016 every 2 weeks. We will check your tumor with MRI scans every 4 weeks to see if it is changing in size. We will also ask you about any side effects you notice from the study drugs and you will have blood tests to monitor for side effects. We may have to stop the drugs if you have serious side effects.

Initial visit to see if you are eligible to participate
We will review your brain MRI scans to see if your GBM has returned and its location. You may need to have another MRI scan of the brain at Emory. You will have a history and physical exam. You will have blood tests including blood cell counts, clotting and blood chemistries. You will have a chest x-ray and urinalysis. You will have an electrocardiogram (ECG) and echocardiogram. All participants

who can physically become pregnant will have a pregnancy test. You will not be able to be in the study if you are pregnant. These are the tests you will have to see if you are eligible to participate:

History and Physical examination
We will review your medical records and ask you about your medical history. You will have a physical exam. Please note that this physical exam is for research purposes only. It does not replace any exam you may receive from your own physicians.

Electrocardiography (ECG)
The ECG records the electrical activity of the heart. For the ECG, we will place small metal disc or sticky pad electrodes on your chest. You will be asked to lie still for a few minutes while the ECG is recorded.

The echocardiogram uses sound waves to look at the heart. For the echocardiogram, a gel will be placed on your chest. A probe, like a small microphone, will be moved over your chest to look at your heart.

Magnetic Resonance Imaging (MRI)
Magnetic resonance imaging (MRI) uses a strong magnetic field and radio waves to take pictures of your brain. The MRI scanner is a metal cylinder surrounded by a strong magnetic field. You will lie on a table that can slide in and out of the cylinder. You will be in the scanner about 60 minutes. You may be asked to lie still for up to 15 minutes at a time. While in the scanner you will hear loud knocking noises, and you will be fitted with earplugs or earmuffs to muffle the sound. You will be able to communicate with the MRI staff at all times during your scan, and you may ask to be moved out of the machine at anytime.

During part of the MRI, you will receive gadolinium, a contrast agent, through an intravenous (IV) catheter. A needle will be used to guide a thin plastic tube (catheter) into one of your arm veins. The needle will be removed, leaving only the catheter in the vein. The catheter will be taped to the skin to hold it in place.

Blood Drawing
Blood will be drawn through a needle in your arm. We will draw no more than 1 cup of blood at any one time. We will take no more than 2 and a half cups of blood from you in any 8 week period during the study.

Prior to Surgery
If you are eligible and agree to participate, you will be scheduled for hospitalization and surgery. You will have to stop taking some drugs before surgery. You will need to stop any of these drugs at least 7 days before surgery:

- Aspirin (such as Excedrin)
- Nonsteroidal anti-inflammatory medications, like ibuprofen (Advil, Motrin), celecoxib (Celebrex), and diclofenac (Cambria, Voltaren) and others
- Vitamin E or supplements with vitamin E

Other supplements or drugs may have to be held as well. Please let us know about all medicines and supplements you are taking.

Hospitalization and Surgery
You will be admitted to the hospital, usually 1-2 days before surgery.

First Surgery:
The first study surgery is for research purposes only. On the day of the first surgery, you will be taken to the operating room. You will get general anesthesia. We will place a tube into your back (called a "lumbar drain") so that we can collect spinal fluid for a week after surgery. We will then take a biopsy of your brain tumor. The sample will be used to make sure your tumor has come back. Some of the sample may be saved for research use. Next, we will place 2 microdialysis tubes into the brain. One tube will be placed in the tumor. Another tube will be placed near the tumor. The tubes will be placed through small holes in your scalp and skull.

After the surgery, you will be taken to the intensive care unit for monitoring.

A few hours after surgery, you will have a computed tomography (CT) scan of the brain. The CT scan will let us check for bleeding from the surgery and to make sure that the microdialysis tubes are in the right places. CT scanning uses x-rays to obtain an image of the brain. The CT scanner is shaped like a metal cylinder. You will lie on a table that slides in and out of the scanner. You will be in the scanner for about 15 minutes. You may be asked to lie still for up to 10 minutes at a time. You will be able to communicate with the CT staff at all times, and you may ask to be moved out of the machine at any time.

Monitoring in the Intensive Care Unit (ICU) and Inpatient Unit
When people have surgery for a GBM, they usually stay in the ICU for one night after surgery. In this study, you will need to stay in the ICU for 24 hours after the first surgery, and then be transferred to an inpatient room. We will collect fluid from the catheters in your brain every 6 hours and from the catheter in your back once a day. You will be able to walk around between fluid collection but you cannot leave the floor. You will also have blood drawn every day for research purposes. Your lumbar drain could fall out or stop working. If these happen, we will offer to place a new lumbar drain. You can also opt for a lumbar puncture during the second surgery instead.

First Dose of Nivolumab
Two days after surgery, during your 1 week stay in the ICU and inpatient floor, you will get a single dose of nivolumab through an IV. The nivolumab infusion will take 30 minutes. After getting nivolumab, we will watch you closely over the next 3 hours for side effects. We will check your vital signs (blood pressure, breathing, temperature and pulse) frequently. We will ask you how you are feeling. We will collect additional fluid from the catheters in your back (2 times this day). We will draw an extra blood sample for research (2 times this day).

Second Surgery
One week after the first surgery, you will have the second study surgery. You will be taken to the operating room. You will get general anesthesia. Once you are under anesthesia, we will remove the tube from your back. You may need a small stitch to close the hole that the tube went into. Then we

will remove the microdialysis tubes from the brain. We may need to make new cuts into the scalp to remove the tubes.

Next, you will have standard surgery to remove as much of the GBM as possible.

After the second surgery, you will go back to the intensive care unit. Most participants will stay in the ICU for one night after the second surgery. Once you are well enough to leave the ICU, you will be moved to the neurosurgery unit. You will stay in the hospital until you are well enough to leave. Most people stay in the hospital for 3-5 days after surgery.

Outpatient Drug Phase of the Study

Nivolumab and BMS-986016 infusions
Two weeks after the first dose of nivolumab, that you got while you were in the ICU and inpatient floor, you will return to Emory for an outpatient visit. You will come to Emory for outpatient visits every 2 weeks. You will start getting infusions of nivolumab and BMS-986016 through an IV. Nivolumab will be given first. Nivolumab infusion will take 30 minutes. About 15-30 minutes later, you will get BMS-986016. The BMS-986016 infusion will take one hour. You will be monitored closely for side effects during and for 2 hours after the infusions. You will have a physical exam and blood draw at each visit to monitor for effects of these drugs. An ECG may also be done. Each visit to receive nivolumab and BMS-986016 will take about 5 hours. You will have an MRI scan of the brain once a month.

You will continue to receive nivolumab and BMS-986016 every other week until there are signs that the tumor has come back. We will also stop nivolumab and BMS-986016 if you have side effects that would make it unsafe for the infusions to continue.

It is difficult to tell if a brain tumor is responding to immune therapy. We may need to stop the study medications if your MRI looks like the tumor has come back. We may give you steroids while we wait to see if the MRI changes. We may need to perform a biopsy or resection to know whether the tumor has come back again. If we find that the tumor has come back, we will stop the nivolumab and BMS-986016.

Transfer of Care
We would like to continue to follow you even after the study drugs are stopped. We may be able to continue to care for you at Emory under another protocol. You may choose to transfer your care to your own doctors. If you transfer your care outside of Emory, we will continue to contact to you from time-to-time to see how you are doing. We may ask you to send us your medical records. If we stop nivolumab and BMS-986016 because your tumor has returned, we will ask you to return for an MRI and safety check at least 4 weeks after we stop giving you the study drugs.

How will my medicine be provided?
The medicine that you will take will be dispensed by the pharmacy and delivered to the principal investigator or study team member. The research team will provide the medicine to you. If you have questions about the medicine, you should ask the study doctor or study nurse. You may also call the pharmacy at (404) 712-4718 if you have questions about the medicine. The number for the pharmacy is included on your medicine package.

Who owns my study information and samples?
If you join this study, you will be donating your samples and study information. You will not receive any compensation if your samples or information are used to make a new product. If you withdraw from the study, data and samples that were already collected may be still be used for this study.

What are the possible risks and discomforts?

First surgery: Microdialysis tube placement and brain biopsy, and placement of lumbar drain
The microdialysis tube placement and brain biopsy are done during your first surgery under this study. The microdialysis tubes are being placed only for research purposes. You would not have these brain tubes placed if you were not a part of this study. The risks of placing the tubes and doing the brain biopsy are similar. The most serious risk is a bleed in the brain. As with all brain surgery, there is the risk of a blood clot in the brain. This surgery could also cause a blood clot inside the skull that pushes on the brain. The surgery could cause a stroke. There is the risk of an infection in or around the brain and spinal cord. There is a risk of brain injury. The surgery could lead to serious disability or even death.

Complications from surgery can cause symptoms. Please let us know right away if you develop a severe headache, drowsiness, weakness, loss of vision, or difficulty talking. If we are concerned about a complication of surgery, you will have a MRI scan or a CT scan. You will be treated for any complication. Additional surgery might be needed.

The risk of developing a blood clot that requires surgery is about 1% or 1 in 100 patients who have similar surgery. With immediate surgery, improvement is usually complete, but there can be permanent weakness, loss of vision, and speech problems.

The risk of infection is about 1.2% or 12 in 1000 patients who have similar surgery. If you develop an infection, you will receive antibiotics and may need more surgery. The effects of infection are usually temporary but there can be permanent weakness, loss of vision, and speech problems.

There is a risk of a biopsy that misses the lesion. This risk is about 1%. If a biopsy misses the lesion, you may need to have a repeat biopsy. This would carry the additional 1% risk of hemorrhage.

Lumbar Drain and Lumbar Puncture
The lumbar drain will be placed in your back while you are under general anesthesia for the first surgery. It will be removed one week later during the second surgery. You would not have a lumbar drain placed if you were not part of this study. Having the lumbar drain in place can lead to an infection, headache, blood clot or leak of spinal fluid. The tube can also break. These complications could cause pelvic or leg weakness or numbness. You may require additional surgery for a complication related to the lumbar drain. The lumbar drain could stop working or fall out. If so, we will offer to put a new one in. Placing a new lumbar drain in the intensive care unit would also have risks of infection, headache, blood clot or leak of spinal fluid. This can also cause back pain.

If you do not want the lumbar drain replaced, we will need to perform a lumbar puncture during the second surgery. We would do the lumbar puncture while you are asleep. About one-third of people have a headache for a few days after a lumbar puncture. Usually the headache is not severe and improves without treatment other than a mild pain reliever. Headaches lasting longer than 7 days

develop with one in 50 to 200 lumbar punctures and usually improve gradually over 2 weeks. In rare cases, headaches persist longer. Prolonged headaches may be due to persistent leakage of CSF from the area of the lumbar puncture. If your headache is prolonged, you may get a "blood patch." For the blood patch, we will remove blood from a vein in your arm and inject it into the area of your back where the lumbar puncture was performed to seal off the leak of CSF.

Second Surgery: Removal of the brain tumor and research catheters

The second surgery is to remove your tumor and research catheters. The surgery to remove the tumor will be about 8 days later than if you were not in this study. The delay is so that we can get samples and information for the research about your response to a dose of nivolumab. This delay could be longer if there is a problem during the first surgery or over the next week. Your tumor could get worse during this delay. This delay could make the tumor removal surgery harder or more dangerous. Your brain function could become worse because of this delay.

The risks of the second surgery include loss of speech, paralysis, or loss of sensation. The risks depend on where the lesion is located. Removing a small tumor that is not near the parts of the brain that control speech, movement, or sensation has a 1/10 chance (10%) of causing temporary loss of one of these functions and a 4% chance of permanent loss. Removal larger tumor from near parts of the brain that controls speech, movement, or sensation has a 25-50% chance of causing temporary loss of one of these functions and a 10-25% chance of permanent loss of function. Removal of a lesion less than 0.7 centimeters (1/3 inch) from a part of the brain that controls speech, movement, or sensation has a 1/2 chance (50%) of having temporary loss of one of these functions and a 25% chance of permanent loss of function. We cannot remove parts of the tumor that have grown into brain areas that control speech, movement, and sensation because you would permanently lose one or more of these important functions. The risks, based on the size and location of your own tumor, will be discussed with you before your surgery.

Nivolumab and BMS-986016 Infusions

The lists below show the most common and the most serious side effects of nivolumab that we know about so far. BMS-986016 has not been given to very many people. We do not know very much about its possible side effects. We do not know how taking BMS-986016 might interact with nivolumab. The combination of these 2 drugs may make these side effects more severe or more likely. There might be other side effects that we do not yet know about, including serious side effects.

Possible Side Effects of Nivolumab with BMS-986016:

Very common (may affect more than 1 in 10 people)

- Decreased appetite
- Diarrhea (watery, loose or soft stools)
- Nausea
- Feeling tired or weak
- Inflammation of the heart
- Fever
- Constipation
- Cough
- Joint pain
- Shortness of breath

Common (may affect up to 1 in 10 people)

- Skin rash or itching
- Infections of the upper respiratory tract
- Allergic reaction or other reaction to drug infusion
- Underactive thyroid gland, which can cause tiredness or weight gain
- Overactive thyroid gland, which can cause rapid heart rate, sweating and weight loss
- High blood sugar level
- Inflammation of the nerves causing numbness, weakness, tingling or burning pain of the arms and legs
- Headache
- Dizziness
- Blurry vision, dry eyes
- High blood pressure (hypertension)
- Inflammation of the lungs with coughing, difficulty breathing, shortness of breath
- Inflammation of the intestines (colitis)
- Mouth ulcers and cold sores, dry mouth
- Vomiting or stomach pain
- Patches of skin color change (vitiligo), dry skin, redness of the skin
- Hair loss or thinning
- Pain in the muscles, bones and joints
- Swelling (edema)
- Abdominal pain and discomfort
- Anemia (decrease in red or white blood cell counts)
- ALT increased: lab test result associated with abnormal liver function
- AST increased: lab test result associated with abnormal liver function

Uncommon (may affect up to 1 in 100 people)

- Serious lung infection (pneumonia), bronchitis
- Temporary increase in the number of your blood cells (transient leukocytosis)
- Altered levels of body hormones
- Dehydration
- Inflammation of the liver (hepatitis), with yellowing of the skin or eyes (jaundice)
- Nerve damage
- Eye inflammation with pain, redness, or vision problems
- Fast heart rate
- Inflammation of blood vessels
- Fluid around the lungs
- Inflammation of the pancreas
- Severe rashes or psoriasis
- Inflammation of muscles causing pain or stiffness, painful joints
- Inflammation of the kidney, kidney failure
- Pain
- Chest pain

Rare (may affect up to 1 in 1000 people)

- Lymph node inflammation
- Diabetes
- Blockage of bile ducts
- Inflammation of the nerves or muscles with pain, weakness, and paralysis
- Irregular heart beat
- Fluid in the lungs
- Gastritis (inflammation of the stomach), ulcer of the small intestines
- Severe and possibly fatal peeling of the skin (toxic epidermal necrolysis)

History, Physical Examination, Pregnancy Testing, echocardiogram, ECG:
There is minimal medical risk or discomfort from these procedures.

Contrast Agents
Your x-ray, CT or MRI procedure will require the use of a "contrast agent." The contrast agent is a substance that helps the radiologist interpret the images. The contrast agent will be injected by either a hand-held needle or a machine that does the injection. Most contrast agents stay in your body for only a few minutes, but some of them can remain for a few hours or days without any harm to you or anyone near you. Contrast agents are generally quite safe, but any injection involves some risks. The injection could harm a nerve, artery or vein, or cause infection. The contrast agent could affect kidney function or cause an allergic reaction, though these outcomes are rare. The contrast agent could also leak from your veins a little causing swelling and discomfort, that is typically treated with ice packs.

Magnetic Resonance Imaging (MRI)
MRI exams use powerful magnets to create images of the body. In addition to the possible reactions to contrast materials, you may feel claustrophobic while in the magnet, and will hear loud beeping or hammering noises. If you have tattoos or any metal items in your body such as implants, pacemakers, clips or shrapnel, we will do special screening to make sure your MRI scan is done safely.

Radiation-Related Risks
You will be exposed to radiation from CT scans and other x-rays. Some of these procedures are not necessary for your medical care and will occur because you participate in this study. The estimated radiation dose that you will receive is equal to or less than the natural environmental radiation the average person receives in the United States annually. The principal risk associated with a radiation dose is the possibility of developing a radiation-induced cancer later in life. The risk for radiation-induced cancer from this study is negligible.

Gadolinium Enhancement
You may have some discomfort and bruising from the needle insertion for the intravenous (IV) catheter. Some people feel light-headed or faint. The risks of an IV catheter also include bleeding, infection, or skin or vein inflammation with pain and swelling.

Symptoms from the gadolinium contrast are usually mild. Symptoms may include a cold feeling in the arm during injection, a metallic taste, headache, and nausea. In an extremely small number of patients, more severe symptoms have been reported including allergic reactions, shortness of breath,

wheezing, hives, and lowering of blood pressure. You should not receive gadolinium if you previously had an allergic reaction to it. You will be asked about such allergic reactions before a contrast agent is administered.

People with kidney disease are at risk for a serious reaction to gadolinium contrast called "nephrogenic systemic fibrosis" which has resulted in a very small number of deaths. If you are older than 60 or have diabetes, kidney disease or liver disease, a blood test of your kidney function will be done within 4 weeks before any MRI scan with gadolinium contrast. You may not receive gadolinium for a research MRI scan if your kidney function is not normal.

Most of the gadolinium contrast leaves the body in the urine. However, recent studies have found that very small amounts of gadolinium remain in the body, including the brain. Some gadolinium contrast drugs are less likely to remain than others. In this study, we will use the gadolinium contrast drugs that are less likely to remain whenever possible. There is no evidence at this time that the gadolinium that stays in the body causes any health problems.

Blood drawing
You may have some discomfort and bruising from the needle insertion. Some people feel light-headed or faint.

If you are pregnant you will not be permitted to participate in this research study.

Risk to Pregnancy or Fetus
Procedures or drugs used in this study could harm a developing fetus, such as an MRI scan with gadolinium and anesthesia used during surgery. We do not know if the study drugs, nivolumab are BMS-986016 can harm a pregnancy. We do not know if these drugs can hurt a growing fetus. Because of these risks, participants who are physically able to have a baby and those who are able to father a baby must agree to remain completely abstinent from sexual intercourse or use a reliable method of birth control. Those who are able to father a child must use birth control while in this study and for 33 weeks after their last dose of either nivolumab or BMS-986016. Those who are able to have a baby will have to use birth control while in this study until 24 weeks after their last dose of a study drug.

Effective methods of birth control for this study include:

- hormonal contraception (birth control pills, injected hormones or vaginal ring)
- intrauterine device
- barrier methods (condom or diaphragm) used with spermicide
- surgical sterilization (hysterectomy, tubal ligation, or vasectomy)

It is important for you to know that no method of birth control is totally effective in preventing pregnancy except for surgical sterilization (hysterectomy, tubal ligation or vasectomy) or total abstinence from sexual intercourse.

Participants who can get pregnant will have pregnancy testing on entry to the study and during the study. You will not be able to stay in this study if the pregnancy test is positive. If you become pregnant during participation, we will stop nivolumab and BMS-986016. We will refer you to the

Emory OB/Gyn service. They will check your health and give you advice. We will ask if you are willing to continue to have study visits. We will continue to follow you until you are no longer pregnant.

If you father a child while you are in this study, please inform us. We may ask to evaluate your partner and follow her until she is no longer pregnant.

Risks of Storage and Sharing of Data
Even though we will remove information that could identify you from samples and data that are sent to repositories or shared, there is a very small chance that the samples and data could be identified as yours.

It is possible that the researchers will learn something new during the study about the risks of being in it. If this happens, they will tell you about it. Then you can decide if you want to continue to be in this study or not. You may be asked to sign a new consent form that includes the new information if you decide to stay in the study.

Will I benefit directly from the study?
You may benefit from being in this study if nivolumab and BMS-986016 slow the growth of your brain tumors. We do not know if nivolumab and BMS-986016 will have any effect on the tumor. Also, any benefit from the nivolumab or BMS-986016 may not last very long. The tests of the brain's immune response to nivolumab will not directly help you. What we learn from the study may help future patients with GBM.

Will I be compensated for my time and effort?
You will not be offered compensation for being in this study.

What are my other options?
The alternative to being in this study is to receive medical or surgical treatment for your GBM at Emory (if available) or elsewhere. Medical care for GBM that has regrown may include radiation, chemotherapy and/or surgery. You do not have to participate in this trial to receive GBM surgery at the Emory. You may not have to be in this study to receive nivolumab and BMS-986016. You may be able receive these study drugs elsewhere under the care of your own physicians.

Drugs that are FDA-approved for GBM that has regrown include bevacizumab and gliadel wafers. You will not be able to use bevacizumab, gliadel wafers or other drugs for your tumor while you are in this study. You cannot participate in any other treatment or research study for GBM while in this study. We will discuss all of these options with you before you decide whether you want to be in this study.

Taking part in this study, however, may make you unable to participate in some other research studies, if they exclude people who have taken certain treatments. You should discuss this with the researchers if you have concerns. You may wish to research other study options at websites like clinicaltrials.gov and ResearchMatch.org.

How will you protect my private information that you collect in this study?
Whenever possible, a study number, rather than your name, will be used on study records. Your name and other identifying information will not appear when we present or publish the study results.

Certificate of Confidentiality

There is a Certificate of Confidentiality from the National Institutes of Health for this Study. The Certificate of Confidentiality helps us to keep others from learning that you participated in this study. Emory will rely on the Certificate of Confidentiality to refuse to give out study information that identifies you. For example, if Emory received a subpoena for study records, it would not give out information that identifies you.

The Certificate of Confidentiality does not stop you or someone else, like a member of your family, from giving out information about your participation in this study. For example, if you let your insurance company know that you are in this study, and you agree to give the insurance company research information, then the investigator cannot use the Certificate to withhold this information. This means you and your family also need to protect your own privacy.

The Certificate does not stop Emory from making the following disclosures about you:

- Giving state public health officials information about certain infectious diseases,
- Giving law officials information about abuse of a child, elderly person or disabled person.
- Giving out information to prevent harm to you or others.

Giving the study sponsor or funders information about the study, including information for an audit or evaluation.

Storing and Sharing your Information

De-identified data from this study (data that has been stripped of all information that can identify you), may be placed into public databases where, in addition to having no direct identifiers, researchers will need to sign data use agreements before accessing the data. We will remove or code any personal information that could identify you before your information is shared. This will ensure that, by current scientific standards and known methods, it is extremely unlikely that anyone would be able to identify you from the information we share. Despite these measures, we cannot guarantee anonymity of your personal data.

Your data and specimens from this study may be useful for other research being done by investigators at Emory or elsewhere. To help further science, we may provide your deidentified data and/or specimens to other researchers. If we do, we will not include any information that could identify you. If your data or specimens are labeled with your study ID, we will not allow the other investigators to link that ID to your identifiable information.

Medical Record

If you have been an Emory Healthcare patient before, then you already have an Emory Healthcare medical record. If you have never been an Emory Healthcare patient, you do not have one. An Emory Healthcare medical record will be made for you if an Emory provider or facility gives you any services or procedures for this study.

Copies of the consent form/HIPAA authorization that you sign will be put in any Emory Healthcare medical record you have now or any time during the study.

Emory Healthcare may create study information about you that can help with your care. For example, the results of study tests or procedures. These study results will be put in your Emory Healthcare medical record. Anyone who has access to your medical records will be able to have access to all the study information placed there. The confidentiality of the study information in your medical record will be protected by laws like the HIPAA privacy rule. State and federal laws may not protect the research information from disclosure.

Tests and procedures done at non-Emory places may not become part of your Emory medical record. Also, if you decide to be in this study, it is up to you to let your other health providers know.

In Case of Injury

If you believe you have become ill or injured from this research, you should contact Dr. Edjah Nduom at telephone number 404-778-1900. You should also let any health care provider who treats you know that you are in a research study.

If you get ill or injured from being in the study, Emory will help you to get medical treatment. Neither Emory nor the sponsor have set aside money to pay for this medical treatment. Your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurance does not pay, then you will have to pay these costs.

For Emory, the only exception is if it is proven that your injury or illness is directly caused by the negligence of an Emory employee. “Negligence” is the failure to follow a standard duty of care. You do not give up any legal rights you may have by being in this study, including any right to bring a claim for negligence.

Costs

The study sponsor will pay for certain items and services that you may receive if you take part in this study.

You will have to pay for the items or services for which the study sponsor does not pay. The sponsor will not pay for your regular medical care. If you have insurance, Emory will submit claims to your insurance for items and services that the sponsor does not cover. Emory will send in only those claims for items and services that it reasonably believes your insurance will pay and that the sponsor has not paid.

The actual amount that you have to pay depends on whether or not you have health insurance and whether or not that insurance will pay for any research study costs. Generally, insurance companies will not pay for items and services that are required just for a research study. Some insurance companies will not pay for regular medical treatment or treatment for complications if you are in a study. How much you will have to pay for any co-payments, deductibles or co-insurance depends on your plan. Emory and the sponsor will not pay for these costs.

It is a good idea to contact your insurance provider and tell them you want to be in this research study. Ask them what they will pay for and what they will not pay for. You can also ask the study team for help in figuring out what you will have to pay.

If you do not have insurance, Emory will review your case as part of its program for low-income patient care. The standard policies of that program will apply. The program will figure out if you have to pay any costs for taking part in the study and what those costs will be.

Withdrawal from the Study
You have the right to leave a study at any time without penalty.

For your safety, however, you should consider the study doctor's advice about how to go off the study treatment. If you leave the study before the final planned study visit, the researchers may ask you to have some of the final steps done.

The researchers also have the right to stop your participation in this study without your consent for any reason, especially if they believe it is in your best interest or if you were to object to any future changes that may be made in the study plan.

Authorization to Use and Disclose Protected Health Information

The privacy of your health information is important to us. We call your health information that identifies you, your "protected health information" or "PHI." To protect your PHI, we will follow federal and state privacy laws, including the Health Insurance Portability and Accountability Act and regulations (HIPAA). We refer to all of these laws as the "Privacy Rules." Here we let you know how we will use and disclose your PHI for the main study and for any optional studies in which you may choose to participate.

Main Study

PHI that Will be Used/Disclosed:
The PHI that we will use or share for the main research study includes:

- Medical information about you including your medical history and present/past medications.
- Results of exams, procedures and tests you have before and during the study.
- Laboratory test results.

Purposes for Which Your PHI Will be Used/Disclosed:
We will use and share your PHI for the conduct and oversight of the research study. We will use and share your PHI to provide you with study related treatment and for payment for such treatment. We will also use and share your PHI to conduct normal business operations. We may share your PHI with other people and places that help us conduct or carry out the study, such as laboratories, data management centers, data monitors, contract research organizations, Institutional Review Boards (IRBs) and other study sites. If you leave the study, we may use your PHI to determine your health, vital status or contact information.

Use and Disclosure of Your Information That is Required by Law:
We will use and disclose your PHI when we are required to do so by law. This includes laws that require us to report child abuse or abuse of elderly or disabled adults.

Authorization to Use PHI is Required to Participate:

By signing this form, you give us permission to use and share your PHI as described in this document. You do not have to sign this form. If you do not sign this form, you may still receive non-research related treatment.

People Who will Use/Disclose Your PHI:
The following people and groups will use and disclose your PHI in connection with the research study:

- The Principal Investigator and the research staff will use and disclose your PHI to conduct the study and give you study related treatment.
- Emory may use and disclose your PHI to get payment for study related treatment and to run normal business operations.
- The Principal Investigator and research staff will share your PHI with other people and groups to help conduct the study or to provide oversight for the study.
- National Institute of Neurological Disorders and Stroke (NINDS) is the Sponsor of the study. The Sponsor may use and disclose your PHI to make sure the research is done correctly and to collect and analyze the results of the research. The Sponsor may disclose your PHI to other people and groups like study monitors to help conduct the study or to provide oversight for the study.
- The following people and groups will use your PHI to make sure the research is done correctly and safely:
    - Emory offices that are part of the Human Research Participant Protection Program and those that are involved in study administration and billing. These include the Emory IRB, the Emory Research and Healthcare Compliance Offices, and the Emory Office for Clinical Research.
    - Government agencies that regulate the research including: Office for Human Research Protections; Food and Drug Administration; National Institutes of Health (NIH).
    - Public health agencies.
    - Research monitors and reviewer.
    - Accreditation agencies.
    - Study-supporter, Bristol-Myers Squibb.
- Sometimes a Principal Investigator or other researcher moves to a different institution. If this happens, your PHI may be shared with that new institution and their oversight offices. PHI will be shared securely and under a legal agreement to ensure it continues to be used under the terms of this consent and HIPAA authorization.

Optional Study of Data and/or Specimens for Future Research

Authorization for This Use of PHI is Required to Participate in Optional Study, but Not in Main Study:
You do not have to authorize the use and disclosure of your PHI for the optional study. If you do not authorize the use and disclosure of your PHI for the optional study, then you may not participate in the optional research study, but you can still be in the main research study.

Additional People Who Will Use/Disclose Your PHI for Optional Study:
The same people and groups who will use and disclose your PHI for the Main Study will also do so in connection with the optional research study/storage of PHI for future research.

Expiration of Your Authorization
Your PHI will be used until this research study ends.

Revoking Your Authorization
If you sign this form, at any time later you may revoke (take back) your permission to use your information. If you want to do this, you must contact the study team at:

Edjah Nduom, MD
Winship Cancer Institute, Emory University
1365-C Clifton Road NE
Atlanta, GA 30322

At that point, the researchers would not collect any more of your PHI. But they may use or disclose the information you already gave them so they can follow the law, protect your safety, or make sure that the study was done properly and the data is correct. If you revoke your authorization you will not be able to stay in the main study.

Other Items You Should Know about Your Privacy
Not all people and entities are covered by the Privacy Rules. HIPAA only applies to health care providers, health care payers, and health care clearinghouses. If we disclose your information to people who are not covered by the Privacy Rules, including HIPAA, then your information won't be protected by the Privacy Rules. People who do not have to follow the Privacy rules can use or disclose your information with others without your permission if they are allowed to do so by the laws that cover them. The Sponsor, and people and companies working with the Sponsor on this study are not covered by the Privacy Rules. They will only use and disclose your information as described in this Consent and Authorization.

To maintain the integrity of this research study, you generally will not have access to your PHI related to this research until the study is complete. When the study ends, and at your request, you generally will have access to your PHI that we maintain in a designated record set. A designated record set is data that includes medical information or billing records that your health care providers use to make decisions about you. If it is necessary for your health care, your health information will be provided to your doctor.

We may remove identifying information from your PHI. Once we do this, the remaining information will not be subject to the Privacy Rules. Information without identifiers may be used or disclosed with other people or organizations for purposes besides this study.

Contact Information

Contact Dr. Edjah Nduom at 404-778-1900:

- if you have any questions about this study or your part in it,
- if you feel you have had a research-related injury or a bad reaction to the study drug, or
- if you have questions, or concerns about the research

Contact the Emory Institutional Review Board at 404-712-0720 or 877-503-9797 or irb@emory.edu:

- if you have questions about your rights as a research participant.
- if you have complaints about the research or an issue you rather discuss with someone outside the research team.

You may also let the IRB know about your experience as a research participant through our Research Participant Survey at **https://tinyurl.com/ycewgkke**.

Consent and Authorization

Consent and HIPAA Authorization for Optional Study:
Please initial below if you opt to participate in and authorize use and disclosure of your PHI in the optional study/studies previously described:

Optional Study for Future Research

My samples and data may be used for other research projects. This includes those not related to brain tumors.

☐ **Yes** ☐ **No** _____**Initials**

TO BE FILLED OUT BY SUBJECT ONLY

Please **print** your name, **sign**, and **date** below if you agree to be in this research study, and any optional studies you initialed above. By signing this consent and authorization form, you will not give up any of your legal rights. We will give you a copy of the signed form to keep.

_____
Name of Subject

_____ _____ ____:____ am / pm
Signature of Subject **Date** **Time (please circle)**
(18 or older and able to consent)

_____ _____ ____:____ am / pm
Signature of Legally Authorized Representative **Date** **Time (please circle)**

_____
Authority of Legally Authorized Representative or Relationship to Subject

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TO BE FILLED OUT BY STUDY TEAM ONLY

_____
Name of Person Conducting Informed Consent Discussion

_____ _____ ____:____ am / pm
Signature of Person Conducting Informed Consent Discussion **Date** **Time (please circle)**