Protocol Title: Phase II clinical trial of bavituximab with radiation and temozolomide for patients with newly diagnosed glioblastoma

DF/HCC Principal Research Doctor / Institution:

Elizabeth Gerstner, MD / Massachusetts General Hospital

DF/HCC Site-Responsible Research Doctor(s) / Institution(s):

Patrick Wen, MD / Dana-Farber Cancer Institute

Main Consent

A. INTRODUCTION

You are invited to take part in a clinical trial, a type of research study, because you have newly diagnosed glioblastoma. This research study is studying a combination of drugs with radiation as a possible treatment for this diagnosis.

The names of the study drugs involved in this study are:

- Bavituximab
- Temozolomide

For purposes of this research, you will be referred to as a "participant".

It is expected that about 36 people will take part in this research study.

The National Comprehensive Cancer Network (NCCN), a not-for-profit institution, is supporting this research study by providing funding for the research study. Oncologie, Inc., a pharmaceutical company, is supporting this research by providing the study drug Bavituximab.

This research consent form explains why this research study is being done, what is involved in participating in the research study, the possible risks and benefits of participation, alternatives to participation, and your rights as a research participant. The decision to participate is yours. If you decide to participate, please sign and date at the end of this form. We will give you a copy so that you can refer to it while you are involved in this research study. If you choose not to participate in this research study, the research doctors will discuss other treatment options with you and/or refer you back to your primary doctor.

We encourage you to take some time to think this over, to discuss it with other people and your primary doctor, and to ask questions now and at any time in the future.

B. WHY IS THIS RESEARCH STUDY BEING DONE?

This research study is a Phase II clinical trial. Phase II clinical trials test the safety and effectiveness of an investigational drug to learn whether the drug works in treating a specific disease. "Investigational" means that the drug is being studied.

The FDA (the U.S. Food and Drug Administration) has not approved Bavituximab as a treatment for any disease.

The FDA has approved Temozolomide as a treatment option for your disease.

In this research study, we are studying how the combination of Bavituximab, Temozolomide, and radiation affects your cancer. The current standard care of treatment for newly diagnosed glioblastoma is the combination of Temozolomide and radiation. Temozolomide causes cell death and radiation shrinks and kills the cancer cells. However, radiation also increases the expression of a certain chemical inside cancer cells. This chemical is responsible for stopping the immune system from attacking and killing the cancer cells; Bavituximab binds to this chemical to stop it from doing this. Bavituximab also may activate (cause) the immune system to attack the cancer cells.

C. WHAT OTHER OPTIONS ARE THERE?

Taking part in this research study is voluntary. Instead of being in this research study, you have other options which may include the following:

- Receive standard treatment including Temozolomide in combination with radiation
- Take part in another research study.
- Receive no therapy specific to your cancer.
- Comfort care, also called palliative care. This type of care may help to reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to treat the symptoms.

Please talk to the research doctor about your options before you decide whether you will take part in this research study.

D. WHAT IS INVOLVED IN THE RESEARCH STUDY?

- You will go through 4 separate cycles and receive different combinations of both Bavituximab and Temozolomide. Cycle 1 is 6 weeks and Cycles 2-4 are 4 weeks.
    - In Cycle 1 you will receive radiation on week days, Bavituximab weekly and Temozolomide daily.
    - In Cycle 2 you will receive Bavituximab weekly.
    - In Cycle 3-4 you will receive Bavituximab weekly and Temozolomide monthly.

Your study doctor will discuss with you whether continuing monthly temozolomide alone would be in your best interest.

Sometimes it is hard to keep track of all of the details and procedures that are part of a research study. We will describe them in this consent form and you can refer to this at any time during the research study.

Before the research starts (screening):
After signing this consent form, you will be asked to undergo some screening tests or procedures to find out if you can be in the research study. Many of these tests and procedures are likely to be part of regular cancer care and may be done even if it turns out that you do not take part in the research study. If you have had some of these tests or procedures recently, they may or may not have to be repeated.

- **A medical history,** which includes questions about your health, current medications, and any allergies.
- **A physical exam,** which includes your height and weight measurements
- **Vital signs**
- **Performance status**, which evaluates how you are able to carry on with your usual activities.
- **Blood Tests,** up to 12 teaspoons of blood will be collected for routine and research purposes. The blood draws will occur weekly throughout Cycle 1, Week 1 of Cycle 2, Weeks 1 and 3 of Cycles 3 and 4, and coming off study.
- **Electrocardiogram (EKG),** which measures your heart's electrical activity

- **An assessment of your tumor** by one or more of the following standard assessment tools: MRI (Magnetic Resonance Imaging)

If these tests show that you are eligible to participate in the research study, you may begin the study treatment. If you do not meet the eligibility criteria, you will not be able to participate in this research study.

Study Treatment Overview:

- **Radiation:** You will receive radiation Monday through Friday during cycle 1. This will be administered 1-3 hours after you have taken Temozolomide.

- **Oral Study Drug(s):** The first study treatment cycle lasts 6 weeks and all other cycles last 4 weeks. During this time you will be taking the study drug temozolomide once a day during Cycle 1 and only on days 1-5 during Cycles 3-4.
- **Infused Study Drug(s):** You will be given Bavituximab once a week into your vein (by intravenous infusion) over about 90 minutes. This will continue for up to 4 cycles.
- **Pre-medications:** You may be pre-medicated with drugs to reduce the chance of having a sensitivity reaction to the study treatment. If you tolerate the study treatment without a reaction, then pre-medications may be changed by your doctor.
    - When you are administered Bavituximab you will be pre-medicated with hydrocortisone IV and diphenhydramine IV
    - When you are administered Temozolomide you will be pre-medicated with zofran or other anti-emetic as needed
- **Drug Diary for Temozolomide:** The doctor will look at your drug diary weekly during Cycle 1 and once a month for Cycles 3 and 4.

Each clinic visit (not including Bavituximab infusion) will be 20 to 30 minutes.

If you take part in this research study you will be given a drug diary. You will be asked to document information in the drug diary about the study treatment you are being asked to take.

Research Study Plan:

	Pre-Study	Cycle 1						Off Study
		Wk 1	Wk 2	Wk 3	Wk 4	Wk 5	Wk 6	
Medical History	X	X		X			X	X
Physical Exam	X	X		X			X	X
Vital Signs	X	X	X	X	X	X	X	X
Performance Status	X	X		X			X	X
Blood Tests	X	X	X	X	X	X	X	X
EKG	X							
Tumor Measurement	X							X
Collection of Archival Tissue	X							
Temozolomide		X	X	X	X	X	X	
Bavituximab		X	X	X	X	X	X	
Pre-Medications		X	X	X	X	X	X	
Radiation		X	X	X	X	X	X	
Drug Diary for Temozolomide		X	X	X	X	X		

	Cycle 2				Off Study
	Wk 1	Wk 2	Wk 3	Wk 4	
Medical History		X		X	
Physical Exam		X		X	X
Vital Signs	X	X	X	X	X
Performance Status		X		X	X
Blood Tests	X				X
EKG					
Tumor Assessment				X	X
Collection of Archival Tissue					
Temozolomide					
Bavituximab	X	X	X	X	
Pre-Medications	X	X	X	X	
Radiation					
Drug Diary for Temozolomide					

	Cycle 3				Off Study
	Wk 1	Wk 2	Wk 3	Wk 4	
Medical History		X			
Physical Exam		X		X	X
Vital Signs	X	X	X	X	
Performance Status					
Blood Tests	X		X	X	X
EKG					
Tumor Measurement					X
Tumor Assessment					X
Collection of Archival Tissue					
Temozolomide	X				
Bavituximab	X	X	X	X	
Pre-Medications	X	X	X	X	
Radiation					
Drug Diary for Temozolomide	X				

	Cycle 4				Off Study
	Wk 1	Wk 2	Wk 3	Wk 4	
Medical History		X			
Physical Exam		X		X	X
Vital Signs	X	X	X	X	
Performance Status					
Blood Tests	X		X	X	X
EKG					
Tumor Measurement				X	X
Tumor Assessment				X	X
Collection of Archival Tissue					
Temozolomide	X				
Bavituximab	X	X	X	X	
Pre-Medications	X	X	X	X	
Radiation					
Drug Diary for Temozolomide	X				

Planned Follow-up:

We would like to keep track of your medical condition. We would like to do this by either seeing you in the clinic or calling you on the telephone to see how you are doing. Keeping in touch with you and checking your condition helps us look at the long-term effects of the research study.

E. HOW LONG WILL I BE IN THIS RESEARCH STUDY?

You will be in this research study for up to 18 weeks and you may be followed for up to 3 years.

You may be taken off the research study drugs for many reasons including if:

- It is considered to be in your best interest
- The study treatment or procedures are found to be unsafe or ineffective
- There is any problem with following study treatments and procedures
- You are a female and become pregnant or plan to become pregnant
- Your condition worsens
- A decision is made to close the study

- Or for other unforeseen reasons that make it necessary to stop your participation in the research study

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

In addition, you can stop participating in the research study at any time, however, the FDA requires that any information collected up to the point of your withdrawal cannot be removed from the study. If you decide to stop participating in this research study, we encourage you to talk to the research doctor and your primary doctor first.

F. WHAT ARE THE RISKS OR DISCOMFORTS OF THE RESEARCH STUDY?

There are risks to taking part in any research study. One risk is that you may get a study drug that does not help treat your disease or that makes your condition or disease worse. Another risk is that there may be side effects.

All cancer treatments can have side effects, which can range from mild and reversible to severe, long lasting and possibly life-threatening. There is a great deal of variability among side effects of different cancer treatments and between individuals. In a research study, all of the risks or side effects may not be known before you start the study. **You need to tell your doctor or a member of the study team immediately if you experience any side effects.**

Everyone in the research study will be watched carefully for side effects. You will be monitored during the administration of study drugs to keep track of your blood counts and organ function, particularly your kidney and liver function. If you experience side effects, they may go away after you stop taking the study drug. Some side effects can be mild; but others can be long lasting and may never go away. Some may be life-threatening or fatal.

Since the effect of the study drug(s) taken with other medications may not be known, it is important that you tell the research doctor about all prescription and non-prescription drugs, herbal preparations and nutritional supplements that you are taking or planning to take. There may also be some foods that you should avoid while on this research study and your research doctor will review this information with you.

During the research study, you will be notified of newly discovered side effects or significant findings, which may affect your health or willingness to participate.

You may be asked to sign a new consent form that shows that you have been informed of new information relating to this research study.

<u>Risks Associated with Bavituximab</u>:

Frequent (Occurring in greater that 20% of people)

- Feeling like you are going to throw-up (Nausea)
- Losing your hair (Alopecia)
- Feeling tired (Fatigue)
- Diarrhea
- Low red blood cell counts (Anemia)
- Decrease in a certain type of white blood cells, making you more prone to infection (Neutropenia)
- Weakness (Asthenia)

Occasional (Occurring in 10% to 20% of people)

- Cough
- Headache
- Fever (Pyrexia)
- Throwing up (Vomiting)
- Joint pain (Arthralgia)
- Pain in extremity (arms or legs)
- Back Pain
- Abdominal pain
- Chest pain
- Constipation
- Decrease in appetite
- Shortness of breath (Dyspnea)
- Swelling in the arms or legs (Peripheral edema)
- Nose bleeding (Epistaxis)
- A reduction in the number of white cells in the blood (Leukopenia)

Rare (Occurring in 5% to 10% of people)

- Decrease in the number of platelets in your blood, making you more prone to bleeding (Thrombocytopenia)
- The formation of small clots in arteries in the heart and lungs and/or thickening in arteries found in the heart and lungs which may be life threatening.
- Interference with the tests used to monitor some of the medications used to treat the blood clot

- Loss of appetite (Anorexia)
- Increased tear production
- Inflammation of the mucous membrane of the mouth (Stomatitis)
- Infusion related reaction (an allergic or allergic-like reaction to the study drug which typically occurs when the study drug is being given, or immediately afterwards)
- Dizziness

Risks Associated with Temozolomide:

Frequent (Between a 10-50% chance that this will happen):

- Feeling tired, tiredness, weakness
- Hair loss (temporary)
- Difficulty passing stool
- Diarrhea, which is frequent, loose watery stools, which can cause dehydration and may require hospitalization and treatment with intravenous fluids. Severe and prolonged diarrhea can be life-threatening.
- Dizziness
- Muscle weakness
- Difficulty sleeping or falling asleep; unable to sleep
- Memory impairment
- Feeling sick to the stomach, vomiting

Occasional (Between a 1-10% chance that this will happen):

- A low number of white blood cells that may increase the risk of infection. It may become life- threatening. Symptoms of infection may include fever, pain, redness, and/or difficulty breathing.
- Low red blood cell count (anemia) which may cause tiredness and shortness of breath. May require a blood transfusion.
- Headache
- Convulsion or seizure
- Low number of platelets, which may cause bleeding and bruising. Bleeding may be serious or life threatening and may required a blood transfusion.

Rare (Less than a 1% chance that this will happen):

- Allergic reaction which may cause rash, low blood pressure, hives, fever, difficulty breathing, swelling of the face or throat. Allergic reaction may be serious or life threatening.
- Skin irritation, rash

- A second cancer related to the treatment of your first cancer. This usually occurs years after treatment for the first cancer.
- Damage to the bone marrow (irreversible) which may cause infection, bleeding, and may require blood transfusions.
- Severe skin rash with blisters and can involve inside of mouth and other parts of the body

Risks Associated with Radiation:

Likely (More than a 20% chance that this will happen):

- Fatigue
- Skin redness and/or irritation at the treatment site (possible dryness, itching, peeling, and/or blistering)
- Hair loss at the treatment site
- Difficulty swallowing and eating (possible inhaling food and/or liquids into the lungs, which could also result in pneumonia)
- Increased risk of infection, including pneumonia, which may cause fever, pain, redness, and difficulty breathing. Such infections may become life- threatening.
- Mouth and/or throat sores
- Dry mouth
- Changes in taste and/or smell that may be permanent
- Nausea
- Vomiting
- Weight loss
- Thick saliva

Frequent (Between a 3-20% chance that this will happen)*:*

- Underactive thyroid gland (possible weight gain, heart failure, and/or constipation)
- Skin damage, due to radiation which may cause redness, flaking or sloughing of skin in the radiation treatment area
- Neck swelling
- Jawbone damage
- Hearing loss
- Ear pain and/or pressure
- Ear infection
- Hoarseness

Rare (Less than a 3% chance that this will happen)*:*

- Tooth loss and/or cavities
- Sensitive teeth
- Decreased movement or feeling in the arm and hand
- Increased risk of another type of cancer

Cancer research often includes biopsies, scans, x-rays that are also provided as routine care. The following describes the side effects of procedures done only for the purposes of research.

Risks Associated with MRI Scans:
When having an MRI (Magnetic Resonance Imaging) scan, you will lie still on a table that slides into a tunnel slightly wider than your body. People who feel uncomfortable in confined spaces (claustrophobia) may feel uncomfortable in the narrow cylinder. If you feel uncomfortable in confined spaces, please tell your research doctor. Your doctor may give you a medication to make you feel more comfortable. As images are taken, a loud banging noise will be produced. Earplugs or headphones will be available if needed. The MRI can be stopped at any time at your request, but the scan may not be complete.

Risks Associated with Contrast Agents Used During Scans:
There is a small risk with using a contrast agent that is injected into a vein during the MRI. The contrast agent is a special dye that highlights organs, blood vessels or tissue to make them more visible. Depending on the type of contrast agent that is used, it may cause decreased kidney function or worsen kidney function in people who already have decreased kidney function. Therefore, we will monitor your kidney function closely while you participate in this study. If there is any change in your kidney function, we may have to remove you from the study.

Uncommonly, some people have allergic reactions (such as hives and itching) to the contrast agent. Serious reactions (for example, drop in blood pressure, difficulty breathing or severe allergic reaction and death) are rare.

Reproductive Risks:
The drugs used in this research study may affect a fetus. While participating in this research study and for 4 months after, you should not become pregnant or father a baby, and should not nurse a baby. We can provide counseling about preventing pregnancy for either male or female study participants. Let your doctor know immediately if you become pregnant or find out that you are going to be the father of a child.

Non-Physical Risks:
Because of side effects or the time required for tests and clinic visits while you are on this research study, you may be unable to keep up with your normal daily activities.

G. WHAT ARE THE BENEFITS OF THE RESEARCH STUDY?

We do not know if taking part in this study will help you. This study may help researchers learn information that could help people in the future.

H. CAN I STOP BEING IN THE RESEARCH STUDY AND WHAT ARE MY RIGHTS?

You have the right to choose not to sign this form. If you decide not to sign this form, you cannot participate in this research study.
You can stop being in the research study at any time. Tell the research doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop. Leaving the research study will not affect your medical care outside of the research study.

If you choose not to participate, are not eligible to participate, or withdraw from this research study, this will not affect your present or future care and will not cause any penalty or loss of benefits to which you are otherwise entitled.

It is important to tell the research doctor if you are thinking about stopping so your research doctor can evaluate the risks from stopping the drugs.

I. WILL I BE PAID TO TAKE PART IN THIS RESEARCH STUDY?

You will not be paid for participating in this study.

We may use your samples and information to develop a new product or medical test to be sold. The sponsor and hospital may benefit if this happens. There are no plans to pay you if your samples are used for this purpose.

J. WHAT ARE THE COSTS?

Taking part in this research study might lead to added costs to you or your insurance company.

You will not be charged for Bavituximab. It is possible that Bavituximab may not continue to be supplied free for some reason. If this would occur, your research doctor will talk with you about your options.

You or your insurance company will be charged for portions of your care during this research study that are considered standard care, including the following, Temozolomide and radiation. You may be responsible for co-payments and deductibles that are typical for your insurance coverage.

If you have questions about your insurance coverage, or the items you might be required to pay for, please call financial services for information. The contact information for financial services are:

- Brigham and Women's Hospital: (617) 732-5524 or (617) 732-7485
- Dana-Farber Cancer Institute: (617) 632-3455
- Massachusetts General Hospital: (617) 726-2191

The National Cancer Institute provides an online resource to help people participating in cancer clinical trials understand which services their insurance company is required by law to pay. This can be found at the website below or can be provided by the study team:

www.cancer.gov or 1-800-4-CANCER (1-800-422-6237)

K. WHAT HAPPENS IF I AM INJURED OR BECOME SICK BECAUSE I TOOK PART IN THIS RESEARCH STUDY?

If you think you have been injured as a result of taking part in this research study, tell the person in charge of this research study as soon as possible. The research doctor's name and phone number are listed in this consent form.

The treating hospital will offer you the care needed to treat injuries directly resulting from taking part in this research. These treatments will be billed to your insurance company. You will be responsible for deductibles and co-payments. There are no plans to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

We will need to collect certain personal information about you for insurance or payment reporting purposes, such as your name, date of birth, gender, social security number or Medicare identification number and information related to this research study. We may be required to report this information to the Centers for

Medicare & Medicaid Services. We will not use this information for any other purpose.

L. WHAT ABOUT CONFIDENTIALITY?

We will take measures to protect the privacy and security of all your personal information, but we cannot guarantee complete confidentiality of study data.

Medical information created by this research study may become part of your hospital medical record and may be forwarded to your primary doctor. Information that does not become part of your medical record will be stored in your study file. It may also become part of a DF/HCC research database. The results of this research study may be published. You will not be identified in publications without your permission.

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.

M. WHOM DO I CONTACT IF I HAVE QUESTIONS ABOUT THE RESEARCH STUDY?

If you have questions about the study, please contact the research doctor or study staff as listed below:

Massachusetts General Hospital

- Elizabeth Gerstner, MD: 617-724-8770

Dana-Farber Cancer Institute

- Patrick Wen, MD: 617-632-2166

24-hour contact: Please contact Massachusetts General Hospital at 617-724-8770 and ask that your doctor be paged.

For questions about your rights as a research participant, please contact a representative of the Office for Human Research Studies at DFCI (617) 632-3029. This can include questions about your participation in the study, concerns about the study, a research related injury, or if you feel/felt under pressure to enroll in this research study or to continue to participate in this research study.

N. FUTURE USE OF DATA AND SPECIMENS

Your personal information and/or biospecimens collected during this study may be stored and used for future research. If so, any personal identifiers will be removed so that the information or samples cannot be linked back to you. As a result, we will no longer be able to identify and destroy them.

Investigators, including investigators from collaborating institutions, can request this data and samples for new research. Samples and data may also be shared with outside non-profit academic investigators as well as with for-profit pharmaceutical investigators or commercial entities, with whom we collaborate.

You will not be asked to provide additional informed consent for the use of your de-identified information or samples in future research.

Future research studies may include genetic research. Your genes are unique to you. At this time, you cannot be identified through this research. There is a risk that you might be reidentified in the future as genetic research progresses.

O. PRIVACY OF PROTECTED HEALTH INFORMATION

Federal law requires Dana-Farber/Harvard Cancer Center (DF/HCC) and its affiliated research doctors, health care providers, and physician network to protect the privacy of information that identifies you and relates to your past, present, and future physical and mental health conditions ("protected health information"). If you enroll in this research study, your "protected health information" will be used and shared with others as explained below.

1. What protected health information about me will be used or shared with others during this research?

- Existing medical records, including mental health records.
- New health information created from study-related tests, procedures, visits, and/or questionnaires

2. Why will protected information about me be used or shared with others?

The main reasons include the following:

- To conduct and oversee the research described earlier in this form;

- To ensure the research meets legal, institutional, and accreditation requirements;
- To conduct public health activities (including reporting of adverse events or situations where you or others may be at risk of harm); and
- To provide the study sponsor with information arising from an adverse event or other event that relates to the safety or toxicity of the drug(s) used in the study and for the purpose of this or other research relating the study drug(s) and their use in cancer;
- To better understand the diseases being studied and to improve the design of future studies; and,
- Other reasons may include for treatment, payment, or health care operations. For example, some medical information produced by this research study may become part of your hospital medical record because the information may be necessary for your medical care. (You will also be given a notice for use and sharing of protected health information.)

3. Who will use or share protected health information about me?

- DF/HCC and its affiliated research doctors and entities participating in the research will use and share your protected health information. In addition, other DF/HCC offices that deal with research oversight, billing or quality assurance will be able to use and share your protected health information.

4. With whom outside of DF/HCC may my protected health information be shared?

While all reasonable efforts will be made to protect the confidentiality of your protected health information, it may also be shared with the following entities:

- Outside individuals or entities that have a need to access this information to perform functions relating to the conduct of this research such as analysis by outside laboratories on behalf of DF/HCC and its affiliates (for example, data storage companies, insurers, or legal advisors).
- The sponsor of the study, its subcontractors, representatives, business partners, and its agent(s): DF/HCC
- The funder(s) of the study, its subcontractors, representatives, business partners, and its agent(s): NCCN and Oncologie, Inc.
- Other research doctors and medical centers participating in this research, if applicable

- Federal and state agencies (for example, the Department of Health and Human Services, the Food and Drug Administration, the National Institutes of Health, and/or the Office for Human Research Protections), or other domestic or foreign government bodies if required by law and/or necessary for oversight purposes. A qualified representative of the FDA and the National Cancer Institute may review your medical records.
- Hospital accrediting agencies
- A data safety monitoring board organized to oversee this research, if applicable

Some who may receive your protected health information may not have to satisfy the privacy rules and requirements. They, in fact, may share your information with others without your permission.

5. For how long will protected health information about me be used or shared with others?

- There is no scheduled date at which your protected health information that is being used or shared for this research will be destroyed, because research is an ongoing process.

6. Statement of privacy rights:

- You have the right to withdraw your permission for the research doctors and participating DF/HCC entities to use or share your protected health information. We will not be able to withdraw all the information that already has been used or shared with others to carry out related activities such as oversight, or that is needed to ensure quality of the study. To withdraw your permission, you must do so in writing by contacting the researcher listed above in the section: “Whom do I contact if I have questions about the research study?”
- You have the right to request access to your protected health information that is used or shared during this research and that is related to your treatment or payment for your treatment, but you may access this information only after the study is completed. To request this information, please contact the researcher listed above in the section: “Whom do I contact if I have questions about the research study?”

P. OPTIONAL RESEARCH STUDY:

You are being asked to participate in an optional study. If you decide not to participate in this optional study, you can still participate in the main research study. Please take your time to make your decision and discuss it with others and your primary care physician.

Your participation in this optional research study is voluntary, and you will not be penalized or lose any benefits if you refuse to participate or decide to stop.

Optional Study:

If for some reason you undergo repeat surgeries while you are on treatment we would like to collect additional tumor tissue to analyze and compare to the initial tumor tissue. The additional tumor tissue samples will be used to look at the changes in the immune system's response to the tumor in order to understand how bavituximab is working.

Please indicate whether or not you want to take part in this optional research study.

☐ Not applicable

☐ Yes _____ Initials _____ Date

☐ No _____ Initials _____ Date

Continuing Treatment On Study Beyond 18 Weeks

Only sign this optional consent after 18 weeks of treatment.

You may be able to continue on study treatment after you completed the study (18 weeks of treatment) as long as:

- Your disease and any symptoms did not worsen
- You can tolerate the study
- Your doctor has assessed the potential clinical benefit of continuing treatment and determines that this is in your best interest

If you continue study drug, all foreseeable risks or discomforts and other alternative treatment options as described in the main informed consent form are applicable.

Please indicate your choice to continue treatment on study beyond 18 weeks as described above.

I agree to continue treatment on study beyond 18 weeks:

☐ Yes _____ Initials _____ Date

☐ No _____ Initials _____ Date

Q. DOCUMENTATION OF CONSENT

My signature below indicates:

- I have had enough time to read the consent and think about participating in this study;
- I have had all of my questions answered to my satisfaction;
- I am willing to participate in this study;
- I have been told that my participation is voluntary and I can withdraw at any time

Signature of Participant
or Legally Authorized Representative

Date

Relationship of Legally Authorized Representative to Participant

To be completed by person obtaining consent:

Adult Participant

The consent discussion was initiated on _____ (date).

Signature of individual obtaining consent: _____

Printed name of above: _____

Date: _____

☐ A copy of this signed consent form will be given to the participant or legally authorized representative.

☐ 1) The participant is an adult and provided consent to participate.

☐ 1a) Participant (or legally authorized representative) is a non-English speaker and signed the translated Short Form in lieu of English consent document:

As someone who understands both English and the language spoken by the participant, I interpreted and/or witnessed, in the participant's language, the researcher's presentation of the English consent form. The participant was given the opportunity to ask questions.

Signature of Interpreter/Witness: _____

Printed Name of Interpreter/Witness: _____

Date: _____

☐ 1b) Participant is physically unable to sign the consent form because:

☐ The participant is illiterate.

☐ The participant has a physical disability.

☐ Other (please describe): _____

The consent form was presented to the participant who was given the opportunity to ask questions and who communicated agreement to participate in the research.

Signature of Witness: _____

Printed Name of Witness: _____

Date: _____

☐ 2) The participant is an adult who lacks capacity to provide consent and his/her legally authorized representative:

- ☐ 2a) gave permission for the adult participant to participate
- ☐ 2b) did not give permission for the adult participant to participate