Combined Consent and Authorization to Participate in a Research Study

Low-dose Intra-arterial Bevacizumab for Edema and Radiation necrosis Therapeutic Intervention (LIBERTI)

INTRODUCTION

You are being asked to participate in a research study. Before agreeing to take part in this study, it is important that you read and understand the following explanation. It describes, the purpose, procedures, benefits, risks and discomforts of the study and the precautions that will be taken. It also describes the alternatives available and your right to withdraw from the study at any time. Participation in this research study is completely voluntary.

WHY ARE YOU BEING INVITED TO TAKE PART IN THIS RESEARCH?

You are being invited to take part in a research study about a medication called bevacizumab (Avastin®). You are being invited to take part in this research study because you are a male or female who is 18 years of age or older, have a condition called radiation necrosis and you currently suffer from severe headache, seizures/or and other neurological problems.

If you volunteer to take part in this study, you will be one of about 10 participants to do so at Norton Healthcare and the University of Kentucky.

WHO IS DOING THE STUDY?

The persons in charge of this study are as follows:

Shervin R Dashti, MD, PhD of Norton Neuroscience Institute, Norton Healthcare and Justin F. Fraser, MD of the University of Kentucky, Department of Neurosurgery.

There may be other people on the research team helping at different times during the study. This study is shared between Norton Healthcare and the University of Kentucky.

WHAT IS THE PURPOSE OF THIS STUDY?

The purpose of this research study is to assess how effective and safe Avastin® is when given in one small dose directly through an artery in the neck for the treatment of radiation necrosis.

The results of this study will be shared with UK Healthcare and Norton Healthcare along with the UK Center for Clinical and Translational Science, the Food and Drug Administration and other federal agencies, if required.

Avastin® is an FDA drug approved for use in treating cancers of the kidney, lung, colon, rectum, cervix, ovary or fallopian tube. It is usually given as part of a combination of cancer medicines. Avastin® may be used to treat radiation necrosis but is not FDA approved for that use. For this purpose it is usually given in standard doses (5-7.5 mg/kg) intravenously (through a vein) every 3 weeks for several months. The use of Avastin® in this study is a one-time small drug dose (2.5 kg/mg) given directly into an artery of the neck following temporary blood-brain-breakdown, is therefore considered to be experimental.

Blood-brain-breakdown: The brain is the only organ known to have its own security system, a network of blood vessels that allows the entry of essential nutrients while blocking other substances. Unfortunately, this barrier is so effective at protecting against the passage of foreign substances that it

often prevents life-saving drugs from being able to repair the injured brain. We administer a type of sugar solution into the arteries of the brain, which temporarily opens this barrier and "tricks" it into allowing medicines to enter.

ARE THERE REASONS WHY YOU SHOULD NOT TAKE PART IN THIS STUDY?

You should not be in this study if you have any of the following:

1. You are not able to understand the study well and cannot give informed consent for your treatment.
2. Are involved in another research study that involves another investigational medication.
3. You have a malignant brain tumor.
4. You have been diagnosed with a bleeding disorder.
5. You are currently taking a blood thinner medication (Ex: Coumadin, Warfarin, Lovenox, Arixtra). The use of aspirin is allowed.
6. You have had an abscess in your gastrointestinal tract, an abdominal fistula or a tear in your gastrointestinal tract within the last 28 days
7. You have an ongoing or active infection
8. You have heart disease (congestive heart failure, unstable chest pain or heart beat)
9. You have had major surgery within the last 4 weeks or plan on having major surgery within 4 weeks of completing this study
10. You are pregnant or breastfeeding
11. You have been diagnosed with HIV
12. You are allergic to Bevacizumab

WHERE IS THE STUDY GOING TO TAKE PLACE AND HOW LONG WILL IT LAST?

The research procedures will be done at Norton Brownsboro Hospital (4960 Norton Healthcare Blvd., Louisville KY, 40241), Norton Neuroscience Institute (4950 Norton Healthcare Blvd., Suite 205, Louisville, KY 40241), and UK Medical Center. Participants in this research study will be observed overnight in the hospital after the procedure. If you agree to be in the study you will be ask to participate in the study for one year and take part in four study visits (including initial clinic visit). Each of these visits is expected to last approximately one hour. On the day of your procedure you will be admitted into the hospital and, following the okay from your study doctor, you will be released the next day.

You will may also be asked to complete two questionnaires over the phone.

WHAT WILL YOU BE ASKED TO DO?

Please see the Study Flow Chart shown below for a list of all tests and procedures that will be done during the study. All tests and procedures listed that are being done for the purpose of this research study are marked as **R**. All tests and procedures that are being done as part of your normal care are marked as **NR**.

After having signed this document you will enter the screening phase of this study. It is only after successfully completing this phase you will be entered into the study.

Study Flow Chart

	Pre-Study	Day 0	Day 1	Week 6	Month 3	Month 6	Month 9	Month 12
Informed Consent	R							
Demographics	NR							
Medical History	NR	NR	NR		NR			NR
Concurrent Medication	NR	NR	NR		NR			NR
Physical Exam	NR	R	R		R			R
Neurological Exam	NR	R	R		R			R
Carotid Angiogram		R						
Osmotic blood-brain-barrier breakdown		R						
Avastin®		R						
HIT – 6 Survey (may be via phone)	R			R	R	R	R	R
MIDAS (may be via phone)	R			R	R	R	R	R
NeuroPsych Testing	R				R			R
CDC HRQOL (survey via phone)	R			R	R	R		R
KPS Functional Status	R		R		R			R
Screening Lab tests	R							
ECG (if needed)[1]	R							
Adverse Event monitoring		R	R	R	R	R	R	R
Urine Pregnancy Test		R						
Brain MRI or CT with or without contrast[2]	R				R			R

1 = ECG will be done in participants who are >45 years old or in any patients with history of cardiac problems
2 = If you cannot undergo a MRI for medical reasons you will have a head CT prior to receiving study drug and then again at Months 3 and Months 12

Medical History (including Allergy History): At the pre-study visit you will be asked about any medicines you have used in the past, if you have had to go to a hospital, if you have any other health problems, and if you had any medical or surgical procedures in the past. You will also be asked if you are allergic to any medicine. Following your acceptance into the study we will review your medical history again at visits Day 0, 1, Month 3 and Month 12.

Current Medications: At the pre-study visit you will be asked about medicines you take right now and when you started taking them. You will also be asked about any medicines you recently stopped taking. Following your acceptance into the study we will review your medical history again at visits Day 0, 1, Month 3 and Month 12.

Physical Examination: At the pre-study visit you will receive an abbreviated physical examination and vital signs (heart rate, blood pressure and body weight) will be collected. Later if you are enrolled into the study you will receive this examination again at Day 0 and 1, Month 3 and Month 12.

Neurological Examination: At the pre-study visit you will receive a detailed neurological examination during screening and then again at Day 0 and 1, Month 3 and Month 12 if you are accepted into the study.

Cerebral Angiogram: Is a procedure that involves inserting a catheter (a straw-like device) into a blood vessel in your leg, and guiding it to the **carotid** or vertebral arteries in the neck with the aid of a special x-ray machine. Contrast dye is injected through the catheter so that x-ray movies of your arteries (the arteries that supply your brain with oxygen-rich blood) are taken. This procedure is considered the best way for imaging the neck and brain vessels.

Avastin® Dosing: If you are selected for entry into the study you will receive Avastin® only once on study Day 0. At this visit, you will be put to sleep by the anesthesiologist.

Your anesthesiologist usually delivers the anesthesia medications through an intravenous line in your arm. Sometimes you may be given a gas that you breathe from a mask. Once you are asleep, the anesthesiologist may insert a tube into your mouth and down your windpipe. The tube ensures that you get enough oxygen and protects your lungs from blood or other fluids, such as stomach fluids. You will be given muscle relaxants before doctors insert the tube to relax the muscles in your windpipe.

Someone from the anesthesia care team monitors you continuously while you sleep. He or she will adjust your medications, breathing, temperature, fluids and blood pressure as needed. Any issues that occur during the surgery are corrected with additional medications and fluids.

As part of standard of care related to the procedure, you will be given certain FDA approved medications as follows:

Valium intravenously – administered to help prevent seizures during the procedure

Mannitol 25% intravenously – administered to will temporarily open the blood–brain–barrier and allow the study drug to get to the brain

Atropine intravenously – administered due to a very small potential risk of slow heart beat during injection of the Mannitol

Dexamethasone intravenously – administered to decrease inflammation

Keppra or Fosphenytoin intravenously – administered to help prevent seizures during the procedure. Fosphenytoin may raise the blood glucose level in diabetic patients. If you are diabetic, please discuss this potential adverse event with Dr. Dashti or a member of the research team.

If you have any questions about these FDA approved medications, please discuss with Dr. Dashti or a member of the research team.

The endovascular surgeon will then use the femoral artery in the leg to thread a plastic catheter all the way into one of the arteries in your neck. Through that catheter, the surgeon will then inject a mannitol sugar solution which will temporarily open the blood–brain–barrier. The endovascular surgeon will then use the same catheter to infuse a very small one-time dose (2.5 mg/kg) of Avastin® into the neck artery over approximately a 15 minute period.

Following the endovascular procedures you will be taken to the recovery unit where your heart rate and oxygen levels will be monitored for 2-4 hours. While in the unit you will have a neurological examination performed every 15 minutes. Once you have recovered from the procedure you will be transferred to the TCU (Transitional Care Unit) or Progressive Care Unit (PCU) or a unit providing a similar level of care, and remain there until you are discharged the following morning.

Questionnaires: You will be asked to complete 2 headache questionnaires. These may be either in person or over the phone. These will be completed at the Pre-study visit and then again at Day 0, Week 6, and months 3, 6, 9 and 12 if you are accepted into the study.
Neuropsychological Testing: These tests will be performed at the Pre-study visit and again at Month 3 and Month 12 if you are accepted into to the study. Each testing session should take one hour to complete.

Karnofsky Performance Status (KPS) Scale: Will be used to measure your neurological functional prior to and following the administration of Avastin®. This test will be performed at the Pre-study visit and again at Day 1, Month 3 and Month 12 if you are accepted into the study.

Screening Lab Tests: Blood will be taken through a vein in your arm in order to determine if it is safe for you to enter into the study. These tests will be performed at the Pre-study visit.

Electrocardiogram (ECG): This test is called an ECG, and it looks at heart rhythm and heart rate. Twelve sticky patches will be put on your chest, arms, and legs for a few minutes, and special wires from a machine will be attached to them. You will lie down or sit in a comfortable position for about 10 to 15 seconds while the machine reads your heart rhythm and heart rate. This tests will be performed at the Pre-study visit.

Pregnancy Testing: You cannot take part in this study if you are pregnant. In order to determine that you are not pregnant, women of childbearing potential will be given a urine pregnancy test at study Day 0 and must agree to abstinence, oral contraception, or barrier contraception for a period of 6 weeks after the procedure.

Brain Magnetic Resonance Imaging (MRI) with and without Contrast: All participants who are medically able will undergo a Brain MRI prior to receiving Avastin®. The MRI will be performed using a contrast called gadolinium. You will receive an MRI at the (Pre-study) and then Months 3 and Month 12 if you are accepted into the study. An MRI is an electronic picture of your brain created using a strong magnet instead of x-ray energy. Each MRI will take approximately 60 minutes to complete. You will lie on your back and enter the MR machine for the study, during which time you may hear loud knocking noises.

CT Scan with or without Contrast: If you cannot have MRI for medical reasons, then a CT Scan of your head will be performed. A CT Scan is a painless test that uses a special X-ray machine to take pictures of a patient's brain, skull, and sinuses, as well as blood vessels in the head.

The doughnut-shaped machine circles the head, taking pictures to provide cross-sections of the brain from various angles. These pictures are sent to a computer that records the images. It can also put them together to form three-dimensional images.

The scan itself generally takes less than 10 minutes. Total time depends on whether contrast solution is given, and whether sedation is needed. Actual exposure time to radiation is much less. If contrast solution is required for the CT scan, it will be given in the radiology area through an IV (intravenous) line placed in your hand or arm.

When the procedure starts, the table moves through the CT machine. You may be asked to your breath for a few seconds to prevent blurring of the image. After the scan is complete, you will be asked to wait

a few minutes so the technician can review the quality of the images. If they are blurred, parts of the CT scan may need to be redone.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

Taking part in this study may involve the following risks:

Avastin®: By participating in this study, you will be getting a one-time administration of low dose (2.5 mg/kg) Avastin directly into the appropriate neck artery. Intravenous Avastin® at conventional dosing (5.0-7.5 mg/kg repeated every 2-4 weeks for several cycles) is associated with risk of GI Perforation (0.3-3.2% incidence), which may be fatal. There is also a small risk of surgery and wound healing complications that may lead to the surgical wound bursting open (dehiscence) and even death. Therefore it is recommended that Avastin not be used for 28 days prior and 28 days after any surgical procedure.

Avastin® has also rarely been associated with severe and sometimes fatal bleeding complications, including, coughing up of blood (hemoptysis), nosebleeds, intestinal, brain, and vaginal bleeding. Other possible major complications of intravenous Avastin® include severe blood clotting abnormality leading to deep venous thrombosis, pulmonary embolus, or venous sinus thrombosis.

The difference in risk of giving Avastin directly into the brain versus the traditional intravenous method is mainly the risk of the cerebral angiogram procedure, which is detailed below. There has been no direct neurotoxicity or brain bleed or stroke seen in previous published cases of Avastin given directly into the brain. Neurotoxicity occurs when exposure to natural or artificial toxic substances, which are called neurotoxins, alters the normal activity of the nervous system in such a way as to cause damage to nervous tissue.

Cerebral angiogram: You may experience the following risks as a result of having this procedure: Heart attack, stroke, injury or tear to the neck or leg artery used during the procedure, irregular heartbeat, and allergic reaction to the iodine based contrast agent or x-ray dye. Sometimes a patient will have a mild reaction to the contrast agent and develop sneezing or hives. Uncommonly (1-2 per 1000), a more serious reaction can occur. Your physicians are trained to treat these reactions. Very rarely (0.9 per 100,000), death has occurred related to contrast media administration. Common side effects including flushed feeling and nausea are not considered allergic reactions. In very rare cases, you may also experience kidney damage, excessive bleeding, or infection.

Please note that pictures in this procedure are taken with x-ray, so you will have some radiation exposure from these X-rays. Your radiation exposure will be greater than that from typical natural background exposure but less than the limit for radiation workers and well below the levels that are considered to be a significant risk of any harmful effects.

Disruption of the blood-brain barrier using a sugar solution: This will be done during the cerebral angiogram procedure immediately before giving Avastin directly into the brain. There is a small chance (less than 5%) of seizure associated with disruption of the blood-brain barrier. A seizure is an uncontrolled electrical activity in the brain, which may produce a physical convulsion, minor physical signs, thought disturbance, or a combination of symptoms.

Magnetic Resonance Imaging (MRI): There are no known risks associated with MRI. An MRI may cause possible anxiety for people due to the loud banging made by the machine and the confined space of the testing area. People with pacemakers, aneurysm clips, artificial heart valves, ear implants or metal/foreign objects in their eyes are not permitted to have an MRI. Intravenous MRI contrast (gadolinium) will be used during this procedure. The most common adverse reactions to this type of contrast are transient mild to moderate headache (4.8%), nausea (2.7%), injection site coldness or localized coldness (2.3%), and dizziness (1%). Anaphylactic (allergic) reactions with heart, lung, and/or skin manifestations resulting in death are rare but have occurred. Also, in patients with kidney

problems, kidney failure requiring dialysis or worsening kidney function have occurred, mostly within 48 hours of contrast injection.

CT Scan: There is some radiation exposure to you during the CT scan. Each CT scan will give a radiation dose greater than that from typical natural background exposure but less than the limit for radiation workers and well below the levels that are considered to be a significant risk of any harmful effects.

ECG: Your skin may become mildly irritated from the sticky patches on your chest. You may feel mildly uncomfortable when the sticky patches are removed, like a band-aid is being peeled off.
Blood draw: Risk associated with blood draws includes, soreness, bruising, pain, infection, possible fainting, bleeding.

General Anesthesia: General anesthesia is overall very safe; most people, even those with significant health conditions, are able to undergo general anesthesia itself without serious problems. Older adults, or those with serious medical problems, particularly those undergoing more extensive procedures, may be at increased risk of postoperative confusion, pneumonia, or even stroke and heart attack. Estimates vary, but about 1 or 2 people in every 10,000 may be partially awake during general anesthesia and experience what is called unintended intraoperative awareness. It is even rarer to experience pain, but this can occur as well. Because of the muscle relaxants given before surgery, people are unable to move or speak to let doctors know that they are awake or experiencing pain. For some patients, this may cause long-term psychological problems, similar to post-traumatic stress disorder.

You'll probably feel groggy and a little confused when you first wake. You may experience common side effects such as:

- Nausea
- Vomiting
- Dry mouth
- Sore throat
- Shivering
- Sleepiness
- Mild hoarseness

Reproductive: It is not known if Avastin® used in this study may cause side effects to pregnant women, to an unborn child, or to children of nursing women. Because of these unknown risks, all women of childbearing potential will be given a pregnancy test prior to receiving study drug. Testing will be performed by urine or blood. Women who are enrolled into this study should not become pregnant during the study or until 6 months following the last dose of study medication (Avastin®).

There is always a chance that any medical treatment can harm you, and the research treatment in this study is no different. In addition to the risks listed above, you may experience a previously unknown risk or side effect.

WILL YOU BENEFIT FROM TAKING PART IN THIS STUDY?

You have the potential of receiving personal benefit from taking part in this study. If the administration of intra-arterial bevacizumab (Avastin®) works as we expect it to, then you may experience improvement of your radiation necrosis related symptoms. There is also the possibility that you may receive no benefit from taking part in this study. Your willingness to take part in this research study, may, in the future help doctors better understand and/or treat patients with your condition.

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any benefits or rights you would normally have if you choose not to volunteer. You can stop at any

time during the study and still keep the benefits and rights you had before volunteering. If you decide not to take part in this study, your decision will have no effect on the quality of medical care you receive.

IF YOU DON'T WANT TO TAKE PART IN THE STUDY, ARE THERE OTHER CHOICES?

If you do not want to be in the study, there are other choices. You may elect to pursue the possibility of an intravenous bevacizumab regimen. You may also be a candidate for other medical treatments for radiation necrosis including steroids, vitamin E, pentoxiphylline, and hyperbaric oxygen. Your study doctor will discuss the risks and benefits of these options with you.

WHAT WILL IT COST YOU TO PARTICIPATE?

You and/or your insurance company, Medicare or Medicaid will be responsible for the costs of all care and treatment you receive during this study that you would normally receive for your condition. These are costs that are considered medically reasonable and necessary and will be part of the care you receive if you do not take part in this study.

The University of Kentucky and Norton Healthcare may not be allowed to bill your insurance company, Medicare or Medicaid for the medical procedures done strictly for research.

There are costs associated with taking part in this study. Either you or insurance company will be responsible for the cost associated with the following. Please refer to the previous page for a listing of when these activities will take place:

- The collection of your demographic, medical history and current medications
- One physical examination
- One neurological examination

All other tests and procedures noted in the noted in the Study Flow Chart are being provided at no cost to you or your insurance company. This includes your overnight hospital stay.\

WHO WILL SEE THE INFORMATION THAT YOU GIVE?

We will make every effort to keep confidential all research records that identify you to the extent allowed by law.

Your information will be combined with information from other people taking part in the study. When we write about the study to share it with other researchers, we will write about the combined information we have gathered. You will not be personally identified in these written materials. We may publish the results of this study; however, we will keep your name and other identifying information private.

We will make every effort to prevent anyone who is not on the research team from knowing that you gave us information, or what that information is. You should know, however, that there are some circumstances in which we may have to show your information to other people. For example, the law may require us to show your information to a court or to tell authorities if you report information about a child being abused or if you pose a danger to yourself or someone else.

In order to process study payments, we will need to collect your social security number. You do not have to provide us with that number however, refusing to provide us with your social security number may result in you not receiving study payments. You can refuse to provide your social security number and still take part in this study.

Your data will be de-identified. A study identifier will consist of the first two letters of your last name and a randomly-generated five-digit number

Research records and source documents will be maintained in a research chart and stored in the investigator's locked file cabinet, or in password-protected electronic files. Charts will not be left in an area where others might have access to them and will not be removed from clinical areas. Information will be kept in a secure database that is password protected.

Electronic and paper charts will only be accessed by approved clinical and research personnel. The study information collected from the subjects participation in the study will be entered into a secure computer system (REDCap). The study information entered into the computer would go directly from the doctor's office to the UK REDCap program through a secure Internet connection. The study sponsor is committed to maintaining the privacy of every study subject and any personal information submitted.

Please be aware, while we make every effort to safeguard your data once received on our servers via REDCap, given the nature of online surveys, as with anything involving the Internet, we can never guarantee the confidentiality of the data while still en route to us.

Only the PI and co-investigators will have access to files matching the subject with their assigned study number.

Officials of the Food and Drug Administration, National Institutes of Health, the University of Kentucky, Norton Healthcare, The Center for Clinical and Translational Research and their contractors, may look at or copy pertinent portions of the records that identify you.

CAN YOUR TAKING PART IN THE STUDY END EARLY?

If you decide to take part in the study you still have the right to decide at any time that you no longer want to continue. You will not be treated differently if you decide to stop taking part in the study.

The individuals conducting the study may need to withdraw you from the study and the study drug and study related treatments will no longer be provided free of charge. This may occur if you are not able to follow the directions they give you, if they find that your being in the study is more risk than benefit to you, or if the agency funding the study decides to stop the study early for a variety of scientific reasons.

ARE YOU PARTICIPATING OR CAN YOU PARTICIPATE IN ANOTHER RESEARCH STUDY AT THE SAME TIME AS PARTICIPATING IN THIS ONE?

You may not take part in this study if you are currently involved in another research study. It is important to let the investigator/your doctor know if you are in another research study. You should also discuss with the investigator before you agree to participate in another research study while you are enrolled in this study.

WHAT HAPPENS IF YOU GET HURT OR SICK DURING THE STUDY?

If you believe you are hurt or if you get sick because of something that is due to the study:

If you are a subject participating at the University of Kentucky in Lexington, KY:
You should call Justin Fraser, MD at (859) 323-0616 immediately during normal working hours. If you become hurt or sick after normal business hours or on the weekend or holiday, please call (859) 257-5522 and ask to speak to Dr. Justin Fraser.

Dr. Fraser will determine what type of treatment, if any, is best for you at that time.

If you are a subject participating at Norton Healthcare in Louisville, KY:
You should call Shervin R. Dashti, MD, PhD at (502) 394-6390 immediately during normal working hours. If you become hurt or sick after normal business hours or on the weekend or holiday, please call

(859) 335-2700 and ask to speak to Dr. Dashti. Dr. Dashti will determine what type of treatment, if any, is best for you at that time.

It is important for you to understand that the University of Kentucky and Norton Healthcare do not have funds set aside to pay for the cost of any care or treatment that might be necessary because you get hurt or sick while taking part in this study. Also, the University of Kentucky and Norton Healthcare will not pay for any wages you may lose if you are harmed by this study.

Your insurance company may or may not be willing to pay for research-related injury treatment costs. If your insurance company does not cover these costs or you have no insurance, the medical costs related to your care and treatment because of research related harm will be your responsibility.

You do not give up your legal rights by signing this form.

WILL YOU RECEIVE ANY REWARDS FOR TAKING PART IN THIS STUDY?

Should you live more than 100 miles from the research facility the study will pay for an overnight stay at a local hotel.

If you earn $600 or more by participating in research, it is potentially reportable for tax purposes.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS, CONCERNS, OR COMPLAINTS?

Before you decide whether to take part in this study, please ask any questions that might come to mind now. Later, if you have questions, suggestions, concerns, or complaints about the study, you can contact the following:

- For UK Healthcare participants please contact Justin Fraser at (859) 323-0616.
- For Norton Healthcare participants please contact Shervin Dashti, MD at (502) 394-6390.

If you have any questions about your rights as a volunteer in this research, contact the staff in the Office of Research Integrity at the University of Kentucky between the business hours of 8am and 5pm EST, Mon-Fri at 859-257-9428 or toll free at 1-866-400-9428. We will give you a signed copy of this consent form to take with you.

WHAT IF NEW INFORMATION IS LEARNED DURING THE STUDY THAT MIGHT AFFECT YOUR DECISION TO PARTICIPATE?

If the researcher learns of new information in regards to this study, and it might change your willingness to stay in this study, the information will be provided to you. You may be asked to sign a new informed consent form if the information is provided to you after you have joined the study.

WHAT ELSE DO YOU NEED TO KNOW?

There is a possibility that the data collected from you may be shared with other investigators in the future. If that is the case the data will not contain information that can identify you unless you give your consent/authorization or the UK Institutional Review Board (IRB) approves the research. The IRB is a committee that reviews ethical issues, according to federal, state and local regulations on research with human subjects, to make sure the study complies with these before approval of a research study is issued.

Norton Healthcare is providing financial support and/or material for this study.

A description of this clinical trial will be available on http://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.

AUTHORIZATION TO USE OR DISCLOSE YOUR IDENTIFIABLE HEALTH INFORMATION

The privacy law, HIPAA (Health Insurance Portability and Accountability Act), requires researchers to protect your health information. The following sections of the form describe how researchers may use your health information.

Your health information that may be accessed, used and/or released includes:

- Demographic information (name, initials, gender, race, age, study number, mailing address, email address and home/work/cell phone numbers and pager number, marital status, insurance information)
- Dates including date of birth, death, hospital admissions/discharges, dates of medical events, study visits
- Medical and medication history as they relate to your enrollment and participation in this study
- Ongoing medication use
- Health Status
- Medical records (as they pertain to this research and your cancer treatment)
- Results of blood tests, other diagnostic and medical procedures
- Hospital and clinic notes and discharge summaries including local practitioner notes and local hospital records
- Pregnancy status

The Researchers may use and share your health information with:

- The University of Kentucky's Institutional Review Board/Office of Research Integrity.
- Law enforcement agencies when required by law.
- University of Kentucky representatives.
- Norton Healthcare representatives.
- UK Hospital if applicable.
- The Food and Drug Administration
- The National Institutes of Health
- Center for Clinical and Translational Science (CCTS)
- Bluegrass Research Consultants, Inc.

The researchers agree to only share your health information with the people listed in this paperwork. Should your health information be given to anyone that is not regulated by the privacy law, your health information may be shared with others without your permission; however, the use of your health information would still be regulated by applicable federal and state laws.

You *will* not be allowed to be in the research study if you do not sign this form. If you decide not to sign the form, it will not affect your:

- **Current or future healthcare at the University of Kentucky or Norton Healthcare**
- **Current or future payments to the University of Kentucky or Norton Healthcare**
- **Ability to enroll in any health plans (if applicable)**
- **Eligibility for benefits (if applicable)**

After signing the form, you can change your mind and NOT let the researcher(s) give out or use your health information (revoke the Authorization). If you revoke the authorization:

- If you are a UK Healthcare participant please send a written letter to:

  Justin Fraser MD

UK Medical Center
Department of Neurosurgery
Medical Science Building Room MS 108A
Lexington, KY 40536-0298

- If you are a Norton Healthcare participant please send a written letter to:

  Shervin R. Dashti, MD, PhD
  4950 Norton Healthcare Blvd. #205
  Louisville, KY 40241

- Researchers may use and give out your health information **already** collected for this research study.
- Your protected health information may still be used and given out to the necessary people should you have a bad reaction (adverse event).
- You may not be allowed to participate in the study.

The use and sharing of your information has no time limit.

If you have not already received a copy of the Privacy Notice, you may request one. If you have any questions about your privacy rights, you should contact the University of Kentucky's Privacy Officer between the hours of 8 am and 5 pm EST, Mon-Fri at: (859) 323-1184 or if you are a Norton Healthcare patient please contact the Norton healthcare Office of Research Administration (NHORA) Director of Research Compliance at (502) 629-3574.

You are the subject. You have read this information, and you will receive a copy of this form after it is signed.

_____
Printed name of subject

_____ _____
Signature of research subject Date Time: _____

_____ _____
I confirm that the study was explained to the participant. I explained the nature and purpose of the study, potential benefits, and possible risks associated with the study. I answered all questions that were raised and witnessed the above signatures.

_____ _____
Name of [authorized] person obtaining informed consent/HIPAA authorization Date

_____
Signature of Investigator or Sub/Co-Investigator