Title: A First-in-Human Clinical Trial of Pharmacologic Ascorbate and Ferumoxytol Combined with Concomitant Temozolomide and External Beam Radiation Therapy for Newly Diagnosed Glioblastoma

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INFORMED CONSENT DOCUMENT

ClinicalTrials.gov Title:	A Safety Study of Pharmacologic Ascorbate and Ferumoxytol in Addition to Standard of Care Chemoradiation in Glioblastoma
IRB Project Title:	A First-in-Human Clinical Trial of Pharmacologic Ascorbate and Ferumoxytol Combined with Concomitant Temozolomide and External Beam Radiation Therapy for Newly Diagnosed Glioblastoma **Group 2: Ferumoxytol twice per treatment period**
Principal Investigator:	Bryan Allen, M.B.A., M.D., Ph.D.
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This consent form describes the research study to help you decide if you want to participate. This form provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights as a research subject.

- If you have any questions about or do not understand something in this form, you should ask the research team for more information.
- You should discuss your participation with anyone you choose such as family or friends.
- Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

What is the purpose of this study?

This is a research study. We are inviting you to participate in this research study because you have a type of brain tumor (glioblastoma) and your doctor has recommended you receive chemotherapy and radiation therapy.

The purpose of this research study is to determine if adding pharmacologic ascorbate (vitamin C) and ferumoxytol (an intravenous iron supplement) is safe and tolerable. We will also study your blood to see if pharmacologic ascorbate and ferumoxytol affect blood components. This is the first study to administer ascorbate and ferumoxytol in addition to the standard treatments of radiation and temozolomide to treat GBM.

Pharmacologic ascorbate as well as ferumoxytol are considered investigational as it is being used in this study. This means it has not been approved by the U.S. Food and Drug Administration for this purpose.

How many people will participate?

Approximately 25 people will take part in this study conducted by investigators at the University of Iowa.

How long will I be in this study?

If you agree to take part in this study, your active involvement will last for up to 35 weeks. You will have lifelong follow-up for this study.

You will receive radiation treatment, combined with chemotherapy, for 6 to 7 weeks. During this time, you will have three extra appointments a week for the ascorbate infusions. This is for the study. Each ascorbate infusion appointment takes about 3 hours. You will also have up to 4 ferumoxytol (iron) infusions. These will add about 1 hour to your visits when they are scheduled.

You will have a one month break after completing your chemo-radiation (before you start your adjuvant chemotherapy). During this month, you will have 2 ascorbate infusions each week. Like before, each study visit will take about 3 hours. You will not receive iron during this month.

You will receive up to 6 cycles of chemotherapy. Each cycle is 28 days (4 weeks). This starts about 1 month after you complete radiation. You will also have ascorbate infusions twice a week during your chemotherapy. Again, each infusion appointment is about 3 hours. During your first cycle of chemotherapy, you will have up to 2 additional ferumoxytol (iron) infusion. Like before, it will add up to 1 hour to your visits.

You will have life-long follow-up for this study. That means when you are no longer receiving the ascorbate or ferumoxytol (the study drugs), we will still want to find out how you are doing. We may visit you during your scheduled cancer treatment appointments or speak with your cancer doctors about how you are doing. If you no longer come to UIHC for your cancer care, we may contact you or any alternative contacts you provide us for this study, the emergency/alternate contact listed in your medical records, or your local physicians to find out how you are doing. If we do not have your current address, we may do an internet-based search to find where you are currently living and may contact you by mail or phone, based on the results of that search.

What will happen during this study?

Before you begin the study treatment

You will need to have some blood tests done to find out if you can be in the study. Some of these tests are part of regular cancer care and may be done even if you do not join the study treatment. If you have had some of them recently, they may not need to be repeated. This is up to your study doctor.

- Blood will be taken to determine blood counts, kidney function, liver function, electrolyte levels, uric acid, coagulation, iron, and levels of an enzyme in your blood called G6PD. These results will be added to your medical record.
- ECG- these results will be added to your medical record
- Pregnancy test (if you are of child-bearing potential). The results of this test will also be added to your medical record.
- You will need an infusion port (Infusaport) for this study. This device allows safe delivery of ascorbate during the infusions; the device is required because repeated high-doses of ascorbate can irritate veins. An Infusaport is a surgically implanted flexible tube that connects to a large vein. It is also called a central venous catheter.

You will need to complete some study tasks before the test dose of ascorbate. If you do not continue with study treatment, the samples, results, imaging, and data will be destroyed and not used.

- T2* MRI. These images are experimental, they are not diagnostic. They will **not** be added to your medical record and cannot be interpreted like normal MRI scans.
- Blood will be taken to determine your baseline ascorbate levels. This is **not** added to your medical record.
- Patient reported outcome measures. You will be asked to complete a questionnaire about how you are feeling and able to perform daily activities. The questionnaire is 31 questions. You can skip any question you would prefer not to answer – simply strike a line through it.

If you agree to the optional studies described later in this consent: We will ask you to complete some study related tasks before the test dose of ascorbate. If you do not continue with study treatment, the samples will be destroyed.

- Research blood sample. This provides a baseline sample for blood components that we think will change due to treatment.

If tests show you can proceed, the last step in screening for the study is a test dose of pharmacologic ascorbate. This dose is 15 grams, about one-sixth of what you will get for treatment. This is to see if you can tolerate the high-dose ascorbate. The results will be added to your medical record.

If you do not tolerate the infusion, or decide to no longer be in the study, the samples, images and data listed above will be destroyed.

<u>During your study treatment: radiation therapy + chemotherapy</u>

If you tolerate the 15g test dose, you will begin chemotherapy, radiation therapy, ferumoxytol and ascorbate infusions. Information about your ferumoxytol infusions and ascorbate infusions, including the dose and your response to it, will be added to your medical record. This means other doctors can see that you are being treated with ferumoxytol and ascorbate.

IMPORTANT. High dose ascorbate may interfere with finger-stick blood glucose readings. **If you are using a finger-stick glucometer, you must discuss this with the study doctor,** as you may not be able to participate in this study.

We will provide you a pocket card you can carry with you. You, or a caregiver, should provide this to a healthcare professional during any treatment you receive away from UIHC.

You will receive the same radiation therapy and chemotherapy you would if you were not in this study:

1. The day before you begin radiation therapy, you will receive your first ferumoxytol infusion. This will be on a Monday, Tuesday, or Wednesday. This will be in the Cancer Center's infusion suite.
2. You will receive radiation therapy once a day, Monday through Friday. You will have breaks for weekends and holidays. Your radiation begins the day after your first ferumoxytol infusion.

3. You will receive temozolomide (chemotherapy) once a day, every day, during your radiation therapy for up to 49 days. You need to take your temozolomide on weekends. Your doctor will tell you when to begin your temozolomide.
4. Each day you take your temozolomide (chemotherapy) we will have you write it on a paper pill diary. We will provide you the pill diary and review it with you.
5. You will get 3 ascorbate infusions each week. Each infusion is 87.5g of ascorbate. It will take at least 2 ½ hours to infuse the ascorbate, so each infusion appointment is about 3 hours.
6. You will complete the health-related quality of life questionnaire weekly. You do not need to answer any questions you choose not to. This will be entered into your medical record and reviewed by our doctor(s).
7. We will draw a blood sample (about 1 tablespoon) after the first ascorbate infusion. This is to check the ascorbate levels in your blood. The results are not added to your medical record.
8. If you do not feel well, or have a reaction to an infusion, you may need to stay longer. If this happens, you will stay until the doctor decides you are able to leave.
9. You will visit your doctors to find out how you are doing. You will see your radiation doctor weekly.
10. You will have blood tests standard for your cancer care. They check how your kidneys, liver, and bone marrow are functioning.
11. You will receive your second ferumoxytol infusion about a week after you begin your radiation.
12. The day after your second ferumoxytol infusion, you will undergo T2* (T2 Star) MRI imaging before your radiation treatment or ascorbate infusion. You will have another T2* MRI about 2-4 hours after your ascorbate infusion.
13. Around the end of your radiation therapy (about week 5 of treatment) you will receive your next set of ferumoxytol infusions. Your study nurses will schedule them for you..
14. The day after your fourth ferumoxytol infusion, you will undergo T2* (T2 Star) MRI imaging before your ascorbate infusion (or, if you are still receiving radiation, before your day's radiation). You will have another T2* MRI about 2-4 hours after your ascorbate infusion.
15. On your T2* MRI imaging day, you will have blood drawn before your radiation treatment or ascorbate to measure iron levels for research (this is not added to your medical record, unless a clinical sample is collected at the same timepoint then the research sample will not be collected).
16. On or around your last radiation therapy treatment, you will have:
    - A blood sample (about 1 teaspoon) drawn after your last ascorbate infusion during radiation therapy. This is to check the ascorbate levels in your blood. This is not added to your medical record.
17. After your radiation therapy ends you will continue to receive ascorbate twice a week for about four to five weeks. This is after radiation therapy but before you start your after-radiation chemotherapy.

During your study treatment: adjuvant chemotherapy

After your radiation therapy, you will receive "adjuvant" chemotherapy. Adjuvant means the chemotherapy is after another type of therapy (radiation therapy). This adjuvant chemotherapy is the same chemotherapy you would receive if you were not in this study. You will receive adjuvant chemotherapy for up to 6 cycles.

1. You will receive temozolomide (chemotherapy) for 5 days and then have a 23 day break. These 28 days are considered one 'cycle' of chemotherapy. You will have an appointment with your doctor before each new cycle of chemotherapy.
2. Like before, you will log each day you take your temozolomide on a pill diary.
3. You will complete the patient questionnaire before each new cycle of chemotherapy. Like before, this will be in EPIC and your doctor(s) will review them. This information is added to your medical record.
4. You will receive ascorbate infusions twice a week for up to 6 cycles of your chemotherapy. They will still be in the HCCC infusion suite or Radiation Oncology. Each infusion appointment is about 3 hours.
5. You will receive your fifth ferumoxytol infusion during the start of your first cycle of temozolomide. We will coordinate this with you so it is the same day you begin your temozolomide.
6. You will receive your sixth, and final, ferumoxytol infusion about 3 to 8 days after you begin your adjuvant cycle 1 temozolomide.
7. The day after your last ferumoxytol infusion, you will undergo T2* MRI imaging like you have before. The MRI sequences are done pre-infusion and then about 4 hours after your ascorbate infusion. This is your last set of T2* images.
8. On your T2* MRI imaging day, you will have blood drawn before your ascorbate infusion to measure iron levels for research (this is not added to your medical record, unless a clinical sample is collected at the same timepoint then the research sample will not be collected).
9. You will have blood tests standard for your cancer care. They check how your kidneys, liver, and bone marrow are functioning. You will have an MRI before cycle 1 of chemotherapy, and then every 2 cycles.
10. During adjuvant cycle 1 around days 22-28 when you have an ascorbate infusion you will have your blood drawn. This is to check the ascorbate levels in your blood. It will not be added to your medical record.

After your study treatment

1. We will schedule a follow-up appointment in the Holden Comprehensive Cancer Center or Radiation Oncology that is about 30 days after your final ascorbate study treatment. That will be your last study-related visit.
2. After that appointment, your active participation in the study is complete. However, we will still follow your progress by reviewing your chart to find out how you are doing. We may also visit you during one of your cancer appointments or contact you by phone. Clinical cancer follow-up visits

are usually scheduled every 3 months. If you no longer use UIHC for your cancer care, we may contact you or your local doctor.

3. If your cancer progresses, your doctors will discuss your further treatment options with you.

End of Study Visit

If you decide to drop out of the study, or if you are withdrawn from the study due to disease progression or a reaction, you will have a final visit with your study doctor. You will need to have some tests done to make sure you are not having side-effects from the therapy. Some of these tests are part of regular cancer care and may be done even if you do not join the study treatment. If you have had some of them recently, they may not need to be repeated. This is up to your study doctor.

- Physical exam, including your weight and vitals (pulse, blood pressure, temperature)
- Patient questionnaire in EPIC
- Blood will be taken to determine blood counts, kidney function, liver function and electrolyte levels

If you are having side effects from the study therapy, you may have additional visits with your study doctor. Your study doctor will discuss this with you. We may also contact you directly to find out how you are doing.

Sometimes, we cannot clearly tell if the tumor has grown. This is called false tumor progression. This can occur with swelling or inflammation, and the MRI looks like the tumor is growing even if it is not. When further surgery is required, sometimes it shows that it is tumor necrosis rather than growing tumor (even though we thought the tumor had grown). If this occurs, and **your doctor believes temozolomide is still your best treatment option**, you may be able to continue or restart the study drug (ascorbate). Your study doctor will decide if this is a treatment option and discuss it with you. You will only receive a total of 6 adjuvant cycles of temozolomide plus ascorbate therapy while on the study. You and your oncologist may decide to continue temozolomide beyond 6 cycles after the study treatment is done.

Surgery

If you require further surgery to treat your tumor, we would like to study a sample of your tumor (if there is any tissue available). We would also like to have you undergo a T2* MRI (like the other MRI) the week of your surgery. Comparing the T2* MRI to the surgery findings is very important to understand what the T2* MRI is showing us.

This is optional. You do not have to choose having your tissue used for research. You also do not have to have the T2* MRI if you do opt to have your tumor tissue used for research.

If I undergo future surgeries for the treatment of my tumor, my tumor tissue can be used for research (if available).

_____ Yes _____ No

I choose to undergo an additional T2* MRI prior to my surgery. I will not be charged for this T2* MRI.

_____ Yes _____ No

Optional: Research Blood Samples

We want to know how the cancer treatments affect your body in addition to the standard clinical tests your doctors order. We are interested in learning if there is a molecule or marker (biomarker) that can predict how the treatment works for patients. In the future, this information may help patients and doctors as they decide which medicines to use to treat cancer.

We are asking you provide about 1 to 2 teaspoons of blood at the following times:

- Before starting treatment
- Before starting temozolomide after radiation (before adjuvant cycle 1)
- About 7 days after completing adjuvant cycle 1

These samples are different than the blood samples we take to check your ascorbate and iron & ferritin levels.

Just like in the main study, we will do our best to make sure that your personal information will be kept private.

Please initial your answer.

_____ Yes, I choose to provide a blood sample at each timepoint list above.

_____ No, I choose not to provide a blood sample. This will not affect my treatment under the study or treatment I would otherwise receive.

Tissue, Blood, and Data Storage for Future Use

As part of this study, we are obtaining blood from you. We are also obtaining your medical images (X-rays, CT, MRIs, and PET scans, for example). If you have further surgery, we would also like to get a sample of any tumor tissue. We would like to study your blood, tumor tissue, and medical images in the future, after this study is over as well as the data from this clinical trial. Your sample, information, and/or data may be placed in a central repository or other national repositories sponsored by the National Institutes of Health or other Federal agencies. If this happens, it may be stripped of identifiers (such as name, date of birth, address). Other qualified researchers who obtain proper permission may gain access to your sample and/or data for use in approved research studies that may or may not be related to in the purpose of this study.

The tests we might want to use to study your blood, tumor tissue, medical images, and study data may not even exist at this time. Therefore, we are asking for your permission to store your blood, tumor tissue, medical images, and study data so that we can study them in the future. These future studies will not include genetic testing, including genome wide sequencing.

These future studies may provide additional information that will be helpful in understanding cancer, but it is unlikely that what we learn from these studies will have a direct benefit to you. It is possible that your blood, tumor tissue, medical images, and study data might be used to develop products tests, or discoveries that could be patented and licensed. In some instances, these may have potential commercial value and may be developed by the Investigators, University of Iowa, commercial

companies, organizations funding this research, or others that may not be working directly with this research team. However, donors of blood, tumor tissue, medical images, and study data do not retain any property rights to the materials. Therefore, there are no plans to provide financial compensation to you should this occur.

Your blood, tumor tissue, medical images, and study data will be stored *with a code which may be linked to* your name and UIHC medical record number. If you agree now to future use of your blood, tumor tissue, medical images, and study data but decide in the future that you would like to have it removed from future research, you should contact Dr. Bryan Allen at (319) 356-3693. However, if some research with your blood or medical imaging has already been completed, the information from that research may still be used.

Please place your initials in the blank next to Yes or No for each of the questions below:

My study data may be stored/shared for future research.

_____ Yes _____ No

My blood may be stored/shared for future research.

_____ Yes _____ No

My tumor tissue (if available) may be stored/shared for future research.

_____ Yes _____ No

My medical images may be stored/shared for future research.

_____ Yes _____ No

Will I be notified if my T2* MR Imaging results in an unexpected finding?

The results from the T2* MR imaging we perform in this research study are not the same quality as what you would receive as part of your routine health care. The MR imaging will not be reviewed by a physician who normally reads such results. Due to this, you will not be informed of any unexpected findings. The results of your T2* MR imaging will not be placed in your medical record with your primary care physician or otherwise. If you believe you are having symptoms that may require care, you should contact your primary care physician.

What are the risks of this study?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks we did not anticipate, associated with being in this study.

Research related risks

Ferumoxytol (intravenous iron)

- Headache (2 to 3.4%)
- Nausea (2 to 3%)
- Vomiting (1.5%)
- Dizziness (1.5 to 2.5%)
- Low blood pressure (hypotension) (2.5%)
- Constipation (2.1%)
- Swelling (peripheral edema) (2%)
- Abdominal pain (1.3%)
- Chest pain (1.3%)
- Cough (1.3%)
- Itching (1.3%)
- Fever (1%)
- Diarrhea (1 to 4%)
- Back pain (1%)
- Breathlessness, short of breath (1%)
- Rash (1%)
- Muscle spasms (1%)

Rare but serious

- Severe allergic reactions (hypersensitivity reactions), which could be life-threatening or fatal (0.6%)
- Hypotension (0.3%)
- Iron overload (too much iron in your system)

Intravenous Ascorbate (Vitamin C)

Mild

- Dry mouth/thirst (>35%)
- Chills (thought to be related to the cool temperature of the IV solution) (>35%)
- Transient blood pressure elevation (about 35%). This is an elevation in your blood pressure that resolves within about 30 minutes after the infusion of ascorbate is complete.
- Headache <5%
- Fatigue <5%
- Facial flushing <5%
- Sweating <5%
- Weakness <5%
- Injection site irritation may occur <2%
- Faintness or dizziness may occur with rapid IV administration <5%
- Abdominal pain <5%

- Increase in iron levels which could potentially cause liver damage
- Risk of gout, gout-like symptoms, or exacerbation of existing gout (<2%)

Serious

- Diarrhea <10%
- Seizure associated with infusion <5%
- Nausea or vomiting <5%
- Kidney stones <5%
- Precipitation of cystine, oxalate or urate crystals in the kidney resulting in kidney damage or failure <1%

Infusa-Port

For this study, you will need to get a Port (Infusa-Port). An infusion port makes it easier for healthcare providers to access a vein, decreasing patient discomfort. It also reduces the number of times you will need a needle inserted, as multiple blood tests and treatments can be given with just one needle stick.

When you have the Port placed, you will most likely experience some discomfort and soreness afterwards. That will go away. There is also a small risk of infection, bleeding, or collapsed lung from the Port placement. The doctors and nurses will review with you how to take care of the Port so that risk is reduced.

Glucose Readings

High dose ascorbate (like you are receiving for this study) has been shown to interfere with finger – stick blood glucose readings. It creates a false (fake) high value. This means after you receive the ascorbate infusion, a finger-stick glucometer would show very high levels of blood sugar, even though your blood sugar is normal. This is also true for a urine analysis. Your urine would show high levels of sugar in it because of the ascorbate. We do not know how long these false readings last.

It is important that you tell your doctor right away if another doctor has requested you monitor your blood sugar or test your urine. Also, if you see another doctor, it is important to let him or her know that a finger stick or urinalysis might have false values.

If you or your doctors have questions, please call (319) 356-1616 and ask for the radiation oncology resident on-call. When they connect you, please tell them you are participating in Dr. Allen's Vitamin C GBM study and you have questions about blood sugar levels.

T2* MRI

You may be uncomfortable inside the MRI scanner if you do not like to be in closed spaces ("claustrophobia"). During the procedure, you will be able to talk with the MRI staff through a speaker system. You can tell them to stop the scan at any time. The MRI scanner produces a loud hammering noise, which has produced hearing loss in a very small number of patients. You will be given earplugs to reduce this risk. If you have claustrophobia, you may require medication to help you relax ("sedation"). If you do require medication to relax, you should not drive a car, take part in activities like riding a bike, or perform other similar tasks until the next morning, because the medication(s) can affect your thinking for several hours and can slow down your reflexes

Financial Risk

Not all insurance companies allow participation in clinical trials. Your insurance company may change your co-payments or deny payment if you participate in a clinical trial. To reduce this risk, we will contact your insurance company to determine if they cover clinical trials – but this is not a guarantee of payment. You may also have additional healthcare costs if you have a side effect from the ascorbate.

Radiation Sensitization

You will receive radiation treatments in the course of this study. The radiation treatments are considered standard of care for your condition. This experimental addition of ferumoxytol and ascorbate may also intensify radiation effects on some normal tissues, and increase risk of radiation-related side effects. Short-term risks include skin changes such as redness, hair loss, or delayed wound healing; and long-term risks include causing a new tumor. The extent to which the risks of radiation therapy will be boosted by the ferumoxytol and ascorbate is not known.

We will closely monitor you for any unforeseen side effects that result from the interaction between the radiation therapy, the chemotherapy, ferumoxytol, and ascorbate (vitamin C).

Confidentiality and Clinical Trials

By participating in a clinical trial, there is the risk of loss of confidentiality of your medical information. We will protect your confidentiality as described in the Confidentiality section of this document.

Individuals Capable of Becoming Pregnant

If you are capable of becoming pregnant, we will ask you to have a pregnancy test before beginning this study. You cannot participate in this study if you are pregnant. You must use effective birth control methods and try not to become pregnant while participating in this study. If you become pregnant, there may be unknown risks to your fetus, or risks to your fetus that we did not anticipate, associated with being in the study. There may be long-term effects of the treatment being studied that could increase the risk of harm to an unborn child. **If you believe or know you have become pregnant while participating in this research study, please contact Bryan Allen, MD at 319-353-8836 as soon as possible.**

What are the benefits of this study?

We don't know if you will benefit from being in this study. However, we hope that, in the future, other people might benefit from this study because of knowledge gained toward finding a better way to treat brain tumors.

What other treatment options are there?

Before you decide whether or not to be in this study, your doctor will discuss the other options that are available to you. Instead of being in this study, you could receive the standard treatment for your tumor (chemotherapy and radiation) or opt to be in a different clinical trial. You could also receive pharmacologic ascorbate outside of the clinical trial at another clinic.

Will it cost me anything to be in this study?

You will have additional costs for being in this research study.

You will not be charged for:

- The ascorbate or the ferumoxytol drugs (the study drugs).
- The glucose-6 phosphatase dehydrogenase (G6PD) test.
- Blood tests to determine the ascorbate levels in your blood. These are not clinical tests and are provided by the study.
- The research iron tests (done with the T2* imaging). These are not clinical tests and are provided by the study.
- The T2* MRI imaging.

However, **you (and your insurance company) will be charged for**:

- Administration (infusion) of the study drugs (ascorbate and ferumoxytol).
- Clinical iron panels and ferritin tests to assess the iron in your blood.
- The placement of the infusion port being used to infuse the study drugs.
- The temozolomide (chemotherapy), this is standard for your cancer.
- The radiation therapy, this is standard for your cancer.
- Your doctors' visits and any other blood tests. You would have those normally for your cancer care.
- Imaging required to plan radiation therapy. This is done once before treatment and during week 4 of your radiation therapy. This is standard for your cancer.

You and/or your medical/hospital insurance carrier will remain responsible for your regular medical care expenses. **You must check with your insurance carrier** about these costs before agreeing to participate. **Some health insurance companies do not allow clinical trial participation.** If your insurance company denies participation in clinical trials, **you are held liable for any charges they will not pay**.

Will I be paid for participating?

You will not be paid for being in this research study.

Who is funding this study?

The National Institutes of Health (NIH) and McGuff Pharmaceuticals, Inc. are funding this research study. This means that the University of Iowa is receiving payments from NIH to support the activities that are required to conduct the study. McGuff Pharmaceuticals is providing the pharmacologic ascorbate at a reduced cost to support this study. No one on the research team will receive a direct payment or increase in salary from NIH or McGuff Pharmaceuticals for conducting this study.

What if I am injured as a result of this study?

- If you are injured or become ill from taking part in this study, medical treatment is available at the University of Iowa Hospitals and Clinics.

- The University of Iowa does not plan to provide free medical care or payment for treatment of any illness or injury resulting from this study unless it is the direct result of proven negligence by a University employee.
- If you experience a research-related illness or injury, you and/or your medical or hospital insurance carrier will be responsible for the cost of treatment.

What about confidentiality?

We will keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

- federal government regulatory agencies,
- Federal government regulatory agencies,
- The U.S. Food and Drug Administration (FDA),
- The National Institutes of Health (NIH),
- The National Cancer Institute (NCI),
- McGuff Pharmaceuticals, Inc.,
- The Holden Comprehensive Cancer Center,
- Auditing departments of the University of Iowa, and
- the University of Iowa Institutional Review Board (a committee that reviews and approves research studies)

To help protect your confidentiality, we will keep study documents and binders in locked offices. Electronic information will be stored on password protected computers. Where feasible, we will use a research ID to minimize using your name. All printed documents are stored in a locked office at the hospital. Any blood and tissue samples that we take for research testing are dated and named using your Research ID. They are also stored at the University in a locked room. If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

The University of Iowa Hospitals and Clinics generally requires that we document your participation in research occurring in a University of Iowa Health Care facility. This documentation will be in either your medical record or a database maintained on behalf of the institution reflecting that you are participating in this study. The information included will provide contact information for the research team as well as information about the risks associated with this study. We will keep this Informed Consent Document in our research files; it will not be placed in your medical record chart.

A description of this clinical trial is available on http://www.ClinicalTrials.gov, as required by U.S. Law. A copy of the informed consent document will be available on this website. 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.

Will my health information be used during this study?

The Federal Health Insurance Portability and Accountability Act (HIPAA) requires your healthcare provider to obtain your permission for the research team to access or create "protected health

information" about you for purposes of this research study. Protected health information is information that personally identifies you and relates to your past, present, or future physical or mental health condition or care. We will access or create health information about you, as described in this document, for purposes of this research study and for your treatment. Once your healthcare provider has disclosed your protected health information to us, it may no longer be protected by the Federal HIPAA privacy regulations, but we will continue to protect your confidentiality as described under "Confidentiality."

We may share your health information related to this study with other parties including federal government regulatory agencies, the University of Iowa Institutional Review Boards and support staff, the U.S. Food and Drug Administration, the National Institutes of Health, McGuff Pharmaceuticals, Inc., and the Data and Safety Monitoring Board of the Holden Comprehensive Cancer Center. McGuff Pharmaceuticals may also inspect any part of your medical record for the purposes of auditing the conduct of the study.

You cannot participate in this study unless you permit us to use your protected health information. If you choose *not* to allow us to use your protected health information, we will discuss any non-research alternatives available to you. Your decision will not affect your right to medical care that is not research-related. Your signature on this Consent Document authorizes your healthcare provider to give us permission to use or create health information about you.

Although you may not be allowed to see study information until after this study is over, you may be given access to your health care records by contacting your health care provider. Your permission for us to access or create protected health information about you for purposes of this study has no expiration date. You may withdraw your permission for us to use your health information for this research study by sending a written notice to:

Bryan G. Allen, M.D., PhD
Department of Radiation Oncology, University of Iowa Hospitals and Clinics
200 Hawkins Drive, Iowa City, IA 52242

However, we may still use your health information that was collected before withdrawing your permission. Also, if we have sent your health information to a third party, such as the study sponsor, or we have removed your identifying information, it may not be possible to prevent its future use. You will receive a copy of this signed document.

Is being in this study voluntary?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I Decide to Drop Out of the Study?

If you decide to leave the study early, we will ask you to discuss your cancer treatment plans with your doctors so that you continue to receive clinical treatment for your cancer. We will ask if there is a specific reason why you no longer want to participate. If you don't want to discuss it, that's okay. If you choose to drop out of the study, you will have an end of study visit described in the section *What will happen during this study?* of this document.

Will I Receive New Information About the Study while Participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can Someone Else End my Participation in this Study?

Under certain circumstances, the researchers might decide to end your participation in this research study earlier than planned. This might happen because your disease has gotten worse or because you had a reaction to the ferumoxytol or ascorbate. If this happens, you will have an end of study visit described in the section *What will happen during this study?* of this document

What if I have questions?

We encourage you to ask questions. If you have any questions about the research study itself, please contact:

Bryan Allen, MD, PhD
Phone number: 319-356-3693

If you believe you are developing any side effects, or are having symptoms that you are concerned about, please contact:

Bryan Allen, MD, PhD
(319) 356-7601 *telephone* (Monday through Friday, 8 a.m. – 5 p.m.)
tell the nurse that you are a participant in Dr. Allen's Iron + Vitamin C study for brain tumors.

If you believe you are experiencing a research-related injury, please contact:

Bryan G. Allen, MD, PhD
(319) 356-7601 *telephone* (Monday through Friday, 8 a.m. – 5 p.m.)

or

(319) 356-1616 (24 hour telephone number)
Ask the operator for the Radiation Oncology resident on call. They will connect you. When you are connected with the fellow, tell them you are a participant in Dr. Allen's Iron + Vitamin C study for brain tumors.

If you have questions, concerns, or complaints about your rights as a research subject or about research related injury, please contact the Human Subjects Office, 105 Hardin Library for the Health Sciences, 600 Newton Rd, The University of Iowa, Iowa City, IA 52242-1098, (319) 335-6564, or e-mail irb@uiowa.edu. General information about being a research subject can be found by clicking "Info for Public" on the Human Subjects Office web site, http://hso.research.uiowa.edu/. To offer input about your experiences as a research subject or to speak to someone other than the research staff, call the Human Subjects Office at the number above.

This Informed Consent Document is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by signing this Informed Consent Document. Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a copy of this form.

Subject's Name (printed): _____

_____ _____
(Signature of Subject) (Date)

Statement of Person Who Obtained Consent

I have discussed the above points with the subject or, where appropriate, with the subject's legally authorized representative. It is my opinion that the subject understands the risks, benefits, and procedures involved with participation in this research study.

_____ _____
(Signature of Person who Obtained Consent) (Date)