# INFORMED CONSENT DOCUMENT

Project Title: **Phase II, Dosimetry guided, Peptide Receptor Radiotherapy (PRRT) using 90Y-DOTA-tyr3-Octreotide (90Y-DOTATOC) in Children and Adults with Neuroendocrine and Other Somatostatin Receptor Positive Tumors**

**Principal Investigator:** **M. Sue O'Dorisio, MD, PhD 319-356-3595 / pager #7444 and Yusuf Menda, MD 319-356-3214 / pager #4352**

**Research Team Contacts:** **Kristin Gaimari-Varner, RN 319-384-5489**

- If you are the parent/guardian of a child under 18 years old who is being invited to be in this study, the word "you" in this document refers to your child. You will be asked to read and sign this document to give permission for your child to participate.
- If you are a teenager reading this document because you are being invited to be in this study, the word "you" in this document refers to you. You will be asked to read and sign this document to indicate your willingness to participate.

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 tumor that expresses somatostatin receptors such as neuroendocrine tumor, medulloblastoma, meningioma, or neuroblastoma. Somatostatin receptors are proteins on a cell that capture hormones from the blood. If there is evidence suggesting your tumor expresses these receptors, we may consider you for participation in this study.

The purpose of this research study is to determine if the study drug 90Y-DOTATOC is an effective treatment for tumors that express somatostatin receptors. 90Y-DOTATOC is a radioactive drug that can cause side effects. This research will also determine if taking a PET/CT radiographic scan of your body between 40-50 hours after your treatment is an effective way to determine how much 90Y-DOTATOC

you can receive while avoiding radiation damage to your kidneys and bone marrow. 90Y-DOTATOC is considered investigational, which means that it has not been approved by the U.S. Food and Drug Administration.

## HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 46 people will participate in this study conducted at the University of Iowa.

## HOW LONG WILL I BE IN THIS STUDY?

Once your eligibility has been confirmed and if you pass the screening tests and agree to take part in this study, your involvement will last for 9 -12 months. During that time you will receive three treatments and have two follow-up visits as described below. Each of the three treatment visits will last 3 days. There will be 6-8 weeks between treatment visits 1 and 2, and another 6-8 weeks between treatment visits 2 and 3. The first follow-up visit will occur approximately 3-4 months following treatment 3 and the last follow-up visit will be between 6-9 months after treatment 3. Each follow-up visit will take 1-2 days.

**Pregnancy Testing for Females Under the Age of 18**

This study uses both external and internal radiation which is dangerous for a fetus. Therefore, all females who are physically able to become pregnant will be required to have a pregnancy test at treatment visits 1, 2 and 3. If the test shows that you are pregnant, you will not be able to continue in the study. This testing will occur in a private area without any of your family members with you.

- If you are 12 years of age or older we will only tell you the results of the test.
- You can decide whether or not to tell your parents or guardian the results of the pregnancy test; however, if you are pregnant we will need to tell your parents you cannot continue in the study.
- If the pregnancy test shows that you are pregnant we will ask you whether or not you want us to talk with your parents or guardian about your pregnancy.
- If you are under 12 years of age and the pregnancy test shows that you are pregnant, we are required to report the pregnancy to the proper authorities.

- **IMPORTANT:** No matter how old you are - if we think that your pregnancy may have happened because of abuse, we will tell the proper authorities and your parents or guardian will be told about your pregnancy.

## WHAT WILL HAPPEN DURING THIS STUDY?

**Before starting the study (Pre-screening):**

You will receive this consent form in the mail or by email. Please read this document carefully and let us know if you are interested in participation in this study. If you wish to be screened for eligibility, you

will need to send us the following:

- unstained slides or a block of your tumor and the associated pathology report,
- a CD with your most recent (within the past 132 days) diagnostic CT scan and/or MRI scan that shows the tumor and any metastatic lesions. This CT or MRI is charged to you or your insurance company.
- a CD with your 68Ga-DOTATOC or 68Ga-DOTATATE PET scan which has been obtained within the past 180 days. This PET scan is charged to you or your insurance company.
- medical records with your most recent treatments, laboratory results and physical exam with vital signs. You or your insurance company must pay this treatment or visit and the laboratory tests.

We will review the tumor pathology, CT and/or MRI scans, and the 68Ga-DOTATOC or DOTATATE PET scan. If you are not eligible, we will call you to inform you. If you are likely to be eligible based on this preliminary review, we will schedule your first visit. This visit will be at least 4 weeks after your most recent Sandostatin LAR injection and at least 8 weeks after your most recent lanreotide injection. You may take immediate release Sandostatin until 12 hrs prior to your first treatment.

**Screening: -7 to 0 days before treatment**

- You will have a chance to ask any questions. After your questions have been answered satisfactorily and you choose to participate, you will sign the consent form for this trial as well as for the Iowa Neuroendocrine Tumor Registry.

**<u>Treatment 1</u>**

**Pre-Treatment: Day 0**

- You will have a physical exam with vital signs performed.
- Blood (approximately 2 tablespoons) will be drawn for laboratory tests, including a CBC with differential, AST, ALT, bilirubin, creatinine. You will be asked to provide a urine sample to check for blood in the urine and a pregnancy test will be performed if you are a female of childbearing age.
- You will be asked to fill out a quality of life questionnaire.
- If you are under the age of 18, you will have two IVs placed during your visit to do a test called a nuclear medicine kidney function test. (This test may be required even if you are over the age of 18. Your study nurse will inform you if it is needed). You will have an injection into one of the IVs and then have three blood draws, each less than a teaspoon, taken from the other IV. You or your insurance company will be charged for this test. This test will take 3 hours.
- We will ask you to drink water (1-1/2 times your recommended liquid requirement) for 18 hours prior to and 48 hours after receiving the therapy. We will ask you to keep a diary of the amount of water you drink. If you cannot drink this amount of fluid, you will have an IV placed to give you the fluid you need.

**First Treatment: Day 1**

- We will review your diary to see if you drank enough water.
- You will have an IV placed to be given extra fluids is needed, and then will receive a medicine to prevent nausea.
- A solution containing amino acids will be given for 30 minutes through the IV to protect your kidneys. You will have a blood draw (~2 teaspoons), before receiving your first treatment with 90Y-DOTATOC therapy. The 90Y-DOTATOC will be given through the IV over 15 minutes and then the amino acid solution will be given through that same IV for another 3-4 hours. You will have a blood draw to check your electrolytes during the last hour of the amino acid infusion.
- Following the 90Y-DOTATOC infusion, you will have another blood draw (2 teaspoons). If you are able to drink sufficient fluid, you will be allowed to go to your hotel.
- We will ask you to keep a diary of how much you drink between the time you leave and the time you return, and we will call you the next day (Day 2) to see how you are doing. If you are not able to drink the prescribed amount of fluid, we will ask you to return that same day to be seen by a member of our research team and you may be given IV fluids.
- Day 3 - You will return to the hospital at 40-50 hrs from the time your 90Y-DOTATOC infusion is completed to have a PET/CT scan to take pictures of the radioactivity remaining in your body. We will schedule the time to return once your 90Y-DOTATOC infusion is complete. When this PET/CT has been completed, you may go home.

**Treatment 2 (6-8 weeks after Treatment 1)**

**Pre-treatment: Day 0**

- You will have a physical exam with vital signs performed.
- Blood will be drawn for laboratory tests (~2 tablespoons).
- If you are under 18 or a nuclear medicine kidney function test was required prior to Treatment 1, this same test will be repeated at this visit. You or your insurance company will be charged for this test.
- We will ask you to drink water (1-1/2 times your recommended liquid requirement) for 18 hours prior to and 48 hours after receiving the therapy. If you cannot drink this amount of fluid, you will have an IV placed to give you the fluid you need. We will ask you to keep a diary of the amount of water you drink.

**Second Treatment: Day 1**

- We will review your diary to see if you drank enough water.
- You will have an IV placed to be given extra fluids is needed, and then will receive a medicine to prevent nausea.
- A solution containing amino acids will be given for 30 minutes through the IV to protect the kidneys.
- You will have a blood draw (~2 teaspoons), before receiving your second treatment with 90Y-DOTATOC therapy. The 90Y-DOTATOC will be given through the IV over 15 minutes and then the amino acid solution will be given through that same IV for another 3-4 hours. You will have a blood draw to check your electrolytes during the last hour of the amino acid infusion.
- Following the 90Y-DOTATOC infusion, you will have another blood draw (2 teaspoons). If you

are able to drink sufficient fluid, you will be allowed to go to your hotel.

- We will ask you to keep a diary of how much you drink between the time you leave and the time you return, and we will call you the next day (Day 2) to see how you are doing. If you are not able to drink the prescribed amount of fluid, we will ask you to return that same day to be seen by a member of our research team and you may be given IV fluids.
- You will return to the hospital at 40-50 hrs after your 90Y-DOTATOC infusion to have a PET/CT scan to take pictures of the radioactivity remaining in your body. We will schedule the time to return once your 90Y-DOTATOC infusion is complete. When these scans are complete, you may go home.

**Treatment 3 (6-8 weeks after Treatment 2)**

**Pre-treatment: Day 0**

- You will have a physical exam with vital signs performed.
- Blood will be drawn for laboratory tests.
- If you are under 18 or you required a nuclear medicine kidney function test previously, this same test will be repeated at this visit. You or your insurance company will be charged for this test. This test will take 3 hours.

We will ask you to drink water (1-1/2 times your recommended liquid requirement) for 18 hours prior to and 48 hours after receiving the therapy. If you cannot drink this amount of fluid, you will have an IV placed to give you the fluid you need. We will ask you to keep a diary of the amount of water you drink.

**Third Treatment: Day 1**

- We will review your diary to see if you drank enough water.
- You will have an IV placed to be given extra fluids is needed, and then will receive a medicine to prevent nausea.
- A solution containing amino acids will be given for 30 minutes through the IV to protect the kidneys.
- You will have a blood draw (~2 teaspoons), before receiving your third treatment with 90Y-DOTATOC therapy. The 90Y-DOTATOC will be given through the IV over 15 minutes and then the amino acid solution will be given through that same IV for another 3-4 hours. You will have a blood draw to check your electrolytes during the last hour of the amino acid infusion.
- You will then be allowed to go to your hotel. On Day 2 after Treatment 3, you will be allowed to go home if you have consumed sufficient fluids. If you have not been able to drink sufficient fluid, you will return to the hospital that same day for IV fluids prior to going home.

**First Follow up: 3-4 months after Treatment 3**

During the first follow-up visit the following will be done:

- You will have a physical exam including vital signs.
- Blood will be drawn for laboratory tests (~2 tablespoons). These tests will be charged to you or your insurance company.

- You will fill out a quality of life questionnaire.
- If you are under 18 or required a nuclear medicine kidney function test previously, this test will be repeated at this visit. You or your insurance company will be charged for this test.
- A diagnostic CT scan or MRI scan will be performed. The CT or MRI scan is considered standard of care and will be charged to you or your health insurer.

The first follow-up visit may be done at your local doctor's office. If your serum creatinine blood test is elevated at the visit with your local doctor, you will need to return to the University of Iowa to have a nuclear medicine kidney function (GFR) test done. If you do have this follow-up visit at your local doctor's office, we will mail or email the Quality of Life Questionnaire to you for completion.

**Second Follow up: 6-9 months after Treatment 3**

During the second follow-up visit the following will be done:

- You will have a physical exam including vital signs.
- Blood will be drawn for laboratory tests (~2 tablespoons). These tests will be paid by you or your insurer.
- If you are under 18 or you required a nuclear medicine kidney function test previously, this test will be repeated at this visit. You or your insurance company will be charged for this test.
- A diagnostic CT scan or MRI scan will be performed. The CT or MRI scan is considered standard of care and will be charged to you or your health insurer.
- A 68Ga-DOTATOC or DOTATATE PET/CT will be performed. This test is considered standard of care and will be charged to you or your insurance company.

Imaging and Kidney Function Testing Schedule

| | | | |
|---|---|---|---|
| **Treatment 1** | Pre | 68Ga-DOTATOC /TATE PET/CT<br>Diagnostic CT or MRI | Nuclear medicine kidney function test |
| | Day 1 | 90Y-DOTATOC infusion | Blood draw prior to the 90Y-infusion.<br>Blood draw after the 90Y-DOTATOC infusion. |
| | Day 3 | Return home unless IV fluids needed | 90Y-DOTATOC PET |
| **Treatment 2** | Day 0 Pre | | Nuclear medicine kidney function test |
| | Day 1 | 90Y-DOTATOC infusion | Blood draw prior to the 90Y-infusion.<br>Blood draw after the 90Y-DOTATOC infusion. |
| | Day 3 | Return home unless IV fluids needed | 90Y-DOTATOC PET |
| **Treatment 3** | Day 0 Pre | | Nuclear medicine kidney |

| | | | |
|---|---|---|---|
| | Day 1 | 90Y-DOTATOC infusion | function test<br>Blood draw prior to the 90Y-infusion.<br>Blood draw after the 90Y-DOTATOC infusion. |
| | Day 2 | Return home unless IV fluids needed | |
| **Followup 1 (3-4 months)** | Diagnostic CT or MRI; nuclear medicine kidney function test if required at any time during treatment | | |
| **Followup 2 (6-9 months)** | Diagnostic CT or MRI; 68Ga-DOTATOC or DOTATATE PET/CT ; nuclear medicine kidney function test if required at any time during treatment | | |

If you are an adult, the physical exams and laboratory tests will take place in the Holden Comprehensive Cancer Center. If you are a child, you will go to the Pediatric Specialty Clinic for the physical exams and laboratory tests. All of the imaging studies and treatments will take place in the Department of Radiology.

Long term follow-up will occur through your participation in the Iowa Neuroendocrine Tumor Registry. Data collected from follow-up in that study will be shared with the research team.

## 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 that we did not anticipate, associated with being in this study.

### 90 Y-DOTATOC:

This treatment involves administering a radioactive drug into your blood stream from where it may attach to any cell (cancerous or healthy) that contains a somatostatin receptor or otherwise comes into contact with the radioactive drug such as the kidneys and bladder. Therefore, healthy cells may potentially be killed or damaged by 90Y-DOTATOC. The kidneys contain somatostatin receptors and they also come in contact with 90Y-DOTATOC as it is being excreted. Adults who have received 90Y-DOTATOC have experienced some damage to the kidneys. Some adults have experienced permanent decrease in kidney function, but no adults have required dialysis. No children who have had this drug have experienced any kidney damage. **There is a risk that severe kidney damage could occur which may result in the need for permanent dialysis. Kidney damage may occur as a late effect, months after the last dose of 90Y-DOTATOC. We require you to drink extra fluids for 18 hours before and 48 hours after infusion of the 90Y-DOTATOC to help protect your kidneys from the internal radiation associated with 90Y-DOTATOC. We also give you an infusion of amino acids before and after the 90Y-DOTATOC infusion to protect your kidneys.**

Other healthy cells that contain somatostatin receptors are present in the pancreas, stomach, duodenum,

small intestine, large intestine, pituitary gland and ovaries. No damage to these organs has been seen in the adults who have taken this drug, most likely because normal cells have fewer somatostatin receptors than the tumor cells. Other healthy organs that do not contain somatostatin receptors, but will come in contact with 90Y-DOTATOC include the bladder because any drug that is not bound to tumor cells will be eliminated in your urine.

In adults and children who have been treated with 90Y-DOTATOC side effects that were observed include: nausea, vomiting, fatigue, diarrhea, weight loss, bowel obstruction, reduced red blood cells (anemia), reduced white blood cells (increased chance of infection), and reduced platelets (increased chance of uncontrolled bleeding). These side effects depended on the dose of 90Y-DOTATOC that was received and occurred at the higher doses tested. Two of 1,000 adult patients who received higher doses of 90Y-DOTATOC suffered bone marrow disease and required a bone marrow transplant. All other patients recovered from these side effects after stopping 90Y-DOTATOC. Other possible side effects include elevated liver function tests, pancreatitis, abdominal pain, bowel obstruction and tumor necrosis syndrome (rapid tumor death that releases toxic cellular elements).

An unexpected allergic reaction following the administration of 90Y-DOTATOC or the amino acids may occur and could consist of shortness of breath, wheezing, lowering of blood pressure, fever, chills, hives, itchiness or blood vessel injury. You will be closely monitored for these side effects and treatment will be provided if appropriate.

**Amino Acid infusions:**

Generalized flushing, fever, and nausea have been reported during infusions of amino acid solutions. Local reactions consisting of a warm sensation, redness, inflammation of the vein and blood clotting at the infusion site have also occurred. There is a possibility of blistering of the skin at the site of the injection. Low phosphate levels have been observed in some adult patients. These levels have not been clinically significant and have returned to within normal limits after completion of therapy. Electrolyte disturbances including a high potassium level and slow heart rate have rarely occurred with the amino acid infusion. To prevent this rare occurrence, potassium level and heart rate will be checked during the last 60 minutes of the amino acid infusion and appropriate medical support, such as administration of oral or IV bicarbonate, will be provided if indicated.

**Radiation Risk from Therapeutic 90Y-DOTATOC infusion**

The radiation exposure to the whole body from the 90Y-DOTATOC and especially to certain organs such as the kidneys and bladder will be substantially higher than the radiation exposure allowed for a radiation technician. This dose of radiation could increase the chance you develop a second cancer in the future. It is unknown if the amount of radiation that you will receive from this treatment will cause problems with functioning of other organs in the long term. Using dosimetry, we limit the radiation dose to your kidneys to $\leq$ 23 Gy, according to FDA safety recommendations.

**Women Capable of Becoming Pregnant**

You may not participate in this study if you are pregnant. If you are a woman who is capable of

becoming pregnant, we will ask you to have a pregnancy test before each 90Y DOTATOC therapy. You must tell us if you may have become pregnant within the previous 14 days because the pregnancy test is unreliable during that time. Both men and women must use effective birth control methods and try not to conceive a child while participating in this study. You must use effective birth control methods for eight months following the end of the last treatment. Any females who are nursing must refrain from nursing while on study and for three months following the end of the last treatment. If you become pregnant, there may be unknown risks to you or risks to your fetus that we did not anticipate, associated with being in the study. There are very likely 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 M Sue O'Dorisio, MD, PhD at 319-356-3595 as soon as possible.

## WHAT ARE THE BENEFITS OF THIS STUDY?

We do not know if you will benefit from being in this study. We cannot predict how your tumor will respond.

However, we hope that, in the future, other people might benefit from this study because it will help us learn whether 90Y-DOTATOC therapy could be helpful in treating tumors that express a high level of somatostatin receptors.

## 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 be treated with chemotherapy or with new anti-angiogenic therapy or remain on somatostatin analog therapy.

## WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You will have **additional costs** for being in this research study. Only the costs of the treatment drug, 90Y-DOTATOC, and the 90Y-DOTATOC PET/CT scans at 48 hrs after treatments 1 and 2 will be paid by the study.

You or your insurance company will cover the cost of a diagnostic CT or MRI prior to entering this study, a second diagnostic CT or MRI at your 3-4 month follow-up visit, and a third CT or MRI at 6-9 months after you complete the three treatments.

You or your insurance company will also cover the cost of a 68Ga-DOTATOC or 68Ga-DOTATATE PET scan within 6 months prior to the first 90Y-DOTATOC treatment and at the 6-9 month followup visit.

You or your insurance company will cover the cost of blood tests, nuclear kidney function test, the IV

fluids and amino acids administered during the therapy, and the cost of nursing support during the therapy administration.

Insurance co-payments will be your responsibility and will not be paid by the study; you should check with your insurance company before participating in this study.

If your doctor orders tumor biomarkers, these tests will not be paid by this study. There may be a charge for sending your tumor slides or block to us and for processing those slides as standard of care; these charges will not be paid by the study. Please talk with your study coordinator about the potential costs of this procedure.

You will need to stay in a hotel, Ronald McDonald House or Hope Lodge for 3-4 nights during each treatment visit. Your travel costs, hotel costs, and food during these stays will be your responsibility and will not be paid by the study.

If you withdraw from this study before completing all three treatments and the two followup visits, you or your insurance company will be charged for a required followup visit, including a nuclear kidney function test, a CT or MRI and laboratory tests.

## WILL I BE PAID FOR PARTICIPATING?

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

## WHO IS FUNDING THIS STUDY?

The National Cancer Institute and the Neuroendocrine Tumor Fund are providing funds to support this research study. This means that the University of Iowa is receiving payments from the National Cancer Institute to support the activities that are required to conduct the study. No one on the research team will receive a direct payment or increase in salary from the National Cancer Institute or the University of Iowa 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,
- the U.S. Food and Drug Administration,
- investigators in the Iowa Neuroendocrine Tumor Registry,
- 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 all paper copies of your information in a locked cabinet in an office which is locked when no one is present. Electronic data will be kept on a password-protected computer. You will be assigned a study number and that, along with your initials, will be the only information that identifies you. The master list of names and study numbers will be kept in a locked cabinet. All discussion of the protocol, the risks, possible benefits, and results of your imaging will be conducted in a private setting. No publication of discussion of the results of this study will mention any subject's name, nor will any identifiers be attached or revealed in these discussions.

Any paper report forms, including signed consent forms, are kept in a locked cabinet in the Principal Investigator's office or the Study Coordinators Office which are both kept locked when not occupied. These records are not sent through campus mail.

All records are kept in a password protected file or in the Neuroendocrine Tumor Registry, both of which are password protected. 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 in your medical record chart that you are participating in this study. The information included in the chart 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. All routine medical data will be entered into your electronic medical record. These records are only available to those involved directly with your clinical care.

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.

## WILL MY HEALTH INFORMATION BE USED DURING THIS STUDY?

The Federal Health Insurance Portability and Accountability Act (HIPAA) requires University of Iowa

Health Care 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 health care provider or University of Iowa Health Care 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 government regulatory agencies, the University of Iowa Institutional Review Boards and support staff. The FDA and the National Cancer Institute 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 health care provider or University of Iowa Health Care 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 M Sue O'Dorisio, MD, PhD at the University of Iowa Children's Hospital, 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 come to a close out visit at which we will perform a history and physical exam with vital signs, obtain blood tests and collect urine for testing, including CBC, differential, AST, ALT, bilirubin and conduct a creatinine clearance test or perform a nuclear kidney function test. The results of these tests will be provided to you and your future risks due

to the treatments will be explained to you. You or your insurance company will be charged for a required followup visit, including a nuclear kidney function test, a CT or MRI and laboratory tests.

**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 or the National Cancer Institute might decide to end your participation in this research study earlier than planned. This might happen because in our judgment it would not be safe for you to continue, because your condition has become worse, because you are or became pregnant, because funding for the research study has ended, or because the National Cancer Institute has decided to stop the research.

## WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: M Sue O'Dorisio (319-356-3595). If you experience a research-related injury, please contact: M Sue O'Dorisio (319-356-3595) or Kristin Gaimari-Varner, RN (319-384-5489). You may reach M Sue O'Dorisio (319-855-2151) or Thomas O'Dorisio (319-430-7669) at any time.

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.

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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): _____

**Do not sign this form if today's date is on or after EXPIRATION DATE: 09/17/19.**

| _____ | _____ |
| --- | --- |
| (Signature of Subject) | (Date) |

Parent/Guardian or Legally Authorized Representative's Name and Relationship to Subject:

_____ _____
(Name - printed) (Relationship to Subject - printed)

**Do not sign this form if today's date is on or after** **EXPIRATION DATE: 09/17/19.**

_____ _____
(Signature of Parent/Guardian or Legally Authorized Representative) (Date)

Legally Authorized Representative:
In studies conducted in the state of Iowa, the first person on the list below who is reasonably available and competent must sign as the legally authorized representative even if another person on the list is more conveniently available.

1. The designated proxy (such as a Durable Power of Attorney for Health Care)
2. Court-appointed guardian
3. Spouse (does not include "Common-law" spouse)
4. Adult child
5. Parent
6. Adult sibling

**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)