INFORMED CONSENT DOCUMENT

Project Title: **Impact of Ga-68 DOTATOC PET-CT Imaging in Management of Neuroendocrine Tumors**

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Research Team Contact: **M. Sue O'Dorisio or Yusuf Menda**

- 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 been diagnosed with a tumor such as carcinoid, neuroendocrine tumor, neuroblastoma, Ewing's sarcoma, or brain tumor that has cells which carry somatostatin receptors.

The purpose of this research study is to see if your tumor can be identified using a special procedure called a positron emission tomography (PET) scan and how the results of this imaging procedure will change the management of your tumor. You will have an injection with a radioactive drug called 68Gallium-DOTA-tyr3-Octreotide (68Ga-DOTATOC) that binds to tumor cells that have somatostatin receptors and then have a PET scan. You will then have a "low dose" computed tomography (CT) scan immediately after the PET scan on the same scanner. We believe this special PET/CT scan will be able to see smaller tumors than the indium [In-111] pentetreotide scan (Octreoscan™ is the Brand name for the scan) that is the current standard of care. 68Ga-DOTATOC is considered investigational, which means that it has not been approved by the U.S. Food and Drug Administration. Your physicians will be asked to complete a form prior to the scan that summarizes their understanding of the extent of disease and the current management of the disease without the information from the PET scan with 68Ga-DOTATOC. After the scan is completed, they will be asked if and how the scan will impact the

management of your tumor.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 200 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 involvement will include at least 2 visits and a phone call.

If your doctor believes your tumor has progressed or if you receive treatment for your tumor after visit 2, you may have up to 4 visits and 2 phone calls. You will have an additional visit for a second 68Ga-DOTATOC PET/CT scan which will include a phone call the following day. This second scan will happen only if your doctor believes your tumor has progressed or if you receive treatment for your tumor, and a second 68Ga-DOTATOC PET/CT scan is recommended to determine how well your tumor responded. Each PET/CT scan will require that you spend approximately 3 hours in the UIHC PET Imaging Center. The screening visit and follow-up visits will take between 30 minutes and an hour.

Pregnancy Testing for Females Under the Age of 18

All females who are physically able to become pregnant will be required to have a pregnancy test before each PET scan. 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?

On the initial visit, we will describe the study to you, answer your questions regarding the study and will perform a physical exam.

- **Visit One in Holden Comprehensive Cancer Center or Pediatric Specialty Clinic (approximately 30 min to 1 hour)**
  - Obtain consent
  - Review pathology report with diagnosis of tumor
  - Review previous conventional imaging such as Octreoscan™ or high-resolution, contrast-enhanced CT or MRI showing uptake in tumor or metastatic lesion
  - Record height, weight, blood pressure, heart rate, respirations, temperature, physical exam
  - Evaluate functional status
  - Have blood drawn for pregnancy test if you are of childbearing potential – if clinical routine blood testing is needed this will be at the same time

If review of this information determines you are eligible to continue, you will continue in the study.

- **Visit Two in the PET Imaging Center (this visit may be combined with Visit One and occur on the same day as Visit One); will take approximately 3 hours**
  - Record height and weight
  - Have urine pregnancy test if you are of childbearing potential, not required if a negative serum/urine pregnancy test within one day (which may have been obtained on your first visit).
  - We may give you a medicine, alprazolam (Xanax®) or lorazepam (Ativan®) at least 30 minutes before the PET scan to help you relax
  - Have an intravenous catheter (IV) inserted
  - Receive IV bolus injection of 68Ga-DOTATOC over less than 1 minute
  - Wait approximately 1 hour for the distribution of 68Ga-DOTATOC in your body
  - Have PET/CT scan over approximately 30 minutes
  - Record blood pressure, heart rate, respirations, temperature and assess for adverse events prior to discharge from PET Center (approximately 10-15 min)

- **Phone call to you at your home or on your cell phone the next day:**
  - Discuss any side effects or reactions to PET scans (rash, nausea, headache, fatigue)
  - Answer any questions you may have regarding the study

Visits three and four will happen only if your doctor believes your tumor has progressed or if you receive treatment for your tumor, such as surgery, liver embolization, peptide receptor radiotherapy (PRRT), chemotherapy, biological therapy or radiation therapy and your doctor needs to re-evaluate the tumor status. The second scan must be between 6 – 18 months after the Visit 2 (scan 1).

- **Visit Three in Holden Comprehensive Cancer Center (Optional; 6-18 months after the 1st scan); will take approximately 30 min to 1 hour**
  - Review your history of symptoms, biomarkers, any Octreoscan™ and high-resolution, contrast-enhanced CT or MRI, and any treatment received.

- Record height, weight, blood pressure, heart rate, respirations, temperature, physical exam
- Have blood drawn for pregnancy test if you are of childbearing potential – if clinical routine blood testing is needed this will be done at the same time
- Evaluate functional status

- **Visit Four in the PET Imaging Center (Optional) - (this visit may be combined with Visit Three and occur on the same day as Visit Three), will take approximately 3 hours**
  - Record height and weight
  - Have pregnancy test if you are of childbearing potential, not required if a negative serum test within 24 hours of PET scan
  - We may give you a medicine, alprazolam (Xanax®) or lorazepam (Ativan®) 30 minutes before the PET scan to help you relax
  - Have an IV inserted
  - Receive IV bolus injection of 68Ga-DOTATOC over less than 1 minute
  - Wait approximately 1 hour for the distribution of 68Ga-DOTATOC in your body
  - Have PET/CT scan approximately 30 minutes
  - Record blood pressure, heart rate, respirations, temperature and assess for adverse events prior to discharge from PET Center (approximately 10-15 min)

- **Phone call to you at your home or on your cell phone (Optional)**
  - Discuss any side effects or reactions to PET scans (rash, nausea, headache, fatigue)
  - Answer any questions you may have regarding the study

The PET/CT images for this study will be reviewed by a nuclear medicine physician and will be entered in your medical record.

The following information will be obtained from your medical record: pathology report indicating presence of a tumor; biomarkers that indicate whether your tumor is growing, including any blood work, CT or MRI and an Octreoscan™ showing this tumor, and what treatments you may have had since your last Octreoscan™ and CT or MRI.

There are no further research procedures in this study after you complete the 68Ga-DOTATOC scans and follow-up phone call. We will follow-up your clinical progress from your clinical chart up to 5 years after your 68Ga-DOTATOC PET/CT scan. If you do not receive your follow-up care at the University, we may contact you to ask for the follow-up information. At that time, if you allow us, we may also contact your physician to obtain information on your tumor therapy/follow-up.

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.

There is a small risk of pain, burning, or infection at the site of the blood draws for laboratory tests and

at the site of IV injection of Ga-68 DOTATOC. If you elect to take alprazolam or lorazepam prior to the PET/CT scan, you may experience drowsiness or unclear thinking. You will not be allowed to drive or to operate machinery for 12-24 hrs. after receiving alprazolam or lorazepam. You will need a driver to take you home or to your hotel following either of these two drugs. Children may require sedation or anesthesia to remain still during the PET scanning procedure. The risks of sedation include a reaction to the medication used for sedation or anesthesia. If anesthesia is required, there is a risk of injury to the throat or airways from insertion of the breathing tube.

There is a financial risk to participating in this study. The FDA has previously allowed us to charge the patient or his/her insurance company for the cost of the drug, which is prepared in the UIHC PET Center. The charge to the patient or her/his insurance company is $5,915. The other costs to the patient for being in this study include travel and loss of work hours; each subject will be free to decline participation based on these financial issues.

There may be some emotional/psychological risk of the PET scan showing more widespread tumor than was previously recognized; however, there is also the possibility that the scan will show less tumor than previously thought.

Radiation Risk

The maximum amount of radiation from the research-related radiation procedures in this study is equivalent to approximately 60 % of the annual radiation limit for a medical worker. Long term effects on your health such as cancer cannot be ruled out from this amount of radiation. This dose estimate takes into account only the exposure to research procedures in this project. If you have participated in other research studies involving radiation exposure, you should be aware that the risk of effects from radiation is believed to increase with each exposure you receive (including studies performed as part of your medical care).

PET Scan Risk

The PET/CT scanner is a large machine with a hollow tube that will be used to see how much 68Ga-DOTATOC is taken into your tumor. You will be asked to lie on your back on a special table that slides into the tube. The sides of the tube will be fairly close to your body and you will be in this scanner for approximately 30-35 minutes. We will monitor you closely while you are inside the scanner. You will also be given a call button to press if you would need to speak to us during the scan. The risks from the PET scan include the radiation described above, pain from lying still on the table or a panic attack if you have claustrophobia.

Children may require sedation or anesthesia to remain still during the PET scanning procedure. The risks of sedation include a reaction to the medication used for sedation or anesthesia. If anesthesia is required, there is a risk of injury to the throat or airways from insertion of the breathing tube.

Women Capable of Becoming Pregnant

If you are a woman who is capable of becoming pregnant, we will ask you to have a pregnancy test before beginning this study. 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 Dr. MS O'Dorisio at 319-356-3595 as soon as possible so that counseling can be provided to you. If a false positive pregnancy test is suspected, an obstetrician will be available to help you and the study team determine if you are or are capable of becoming pregnant.

Radiation Exposure in Women Capable of Becoming Pregnant

You may not participate in this study if you are pregnant. If you are capable of becoming pregnant, we will perform a pregnancy test before exposure to research-related radiation. You must tell us if you may have become pregnant within the previous 14 days because the pregnancy test is unreliable during that time.

Radiation Exposure in Women Who are Breast Feeding

You may not participate in this study if you are breast feeding an infant. There is a chance that the 68Ga-DOTATOC could travel to your infant in your breast milk and cause unknown risks to your child.

WHAT ARE THE BENEFITS OF THIS STUDY?

We don't know if you will benefit from being in this study. We may be able to see more tumor lesions (or less) compared to an Octreoscan™. If you receive a second 68Ga-DOTATOC PET/CT scan 12-36 months after your first, we may or may not be able to determine how much response you had to the treatment.

However, we hope that, in the future, other people might benefit from this study because of knowledge gained in determining whether 68Ga-DOTATOC PET/CT scans are more sensitive than the current Octreoscan™ plus high-resolution, contrast-enhanced CT for detecting somatostatin receptor positive tumors and measuring response to treatment.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You will have additional costs associated with being in this research study. You will be required to pay for study procedures that are not part of your regular care. This includes $5,915 for the 68Ga-DOTATOC PET/CT scan and associated costs, and pregnancy testing (if needed). The $5,915 charge includes making the drug, performing the PET/CT, interpreting the results, and sending a report to your doctor.

In some cases, insurance may cover part of the study procedures. It is recommended that you contact your insurance provider in advance to determine if payment for the study procedures will be covered. In the event that your insurance company denies all or part of the study procedures as "non-covered," you will be responsible for the charges. The University of Iowa Hospitals & Clinics has developed a plan for helping you obtain insurance coverage. If necessary, a physician will engage in a peer-to-peer review with your insurance company. This will increase the chances of the costs being covered, but does not guarantee coverage. If the insurance company denies this request, you will be informed of the cost. You may choose to pay or decline to participate in the study.

Medicare cannot be billed for study procedures that are not part of your regular care. If you have Medicare, you will be billed for all study procedures not part of your regular care.

If you are a child with a tumor, study procedures may be paid by either the University of Iowa Tim Dwight Foundation or the University of Iowa Research for the Kids fund. Talk to your study doctor to determine if you may qualify.

In addition, you will be responsible for your travel costs.

You and/or your medical/hospital insurance carrier will remain responsible for your regular medical care expenses, including any biomarker blood tests and other imaging studies.

WILL I BE PAID FOR PARTICIPATING?

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

WHO IS FUNDING THIS STUDY?

The University and the research team are receiving no payments from other agencies, organizations, or companies to conduct this research study.

The University of Iowa Neuroendocrine Tumor Fund in addition to the University of Iowa Tim Dwight Pediatric Brain Tumor Fund are funding this research study. This means that the University of Iowa is receiving payments from the University of Iowa Neuroendocrine Tumor Fund and the University of Iowa Tim Dwight Foundation 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 University of Iowa Neuroendocrine Tumor Fund or the University of Iowa Tim Dwight Foundation 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, including the U.S. Food and Drug Administration,
- auditing departments of the University of Iowa, and
- the University of Iowa Institutional Review Board (a committee that reviews and approves research studies)

In the future, the U.S. Food and Drug Administration may continue to use your health information that is collected as part of this study. The FDA may combine information from this study with the results of other studies to re-analyze the safety and effectiveness of the Ga-DOTATOC PET/CT in the diagnosis, staging, or evaluation of response of tumors such as yours.

To help protect your confidentiality, we will keep all of your health information related to this study in a file that is in a locked cabinet inside a locked room in UIHC. Data related to the PET scans will be kept in a secure archive that can only be accessed with a special identification and password. 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.

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 your health care 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. Once your health care 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.

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 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, 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 U.S. Food and Drug Administration, 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 contact a member of the study team (Names and phone numbers are listed on the front of this consent form). We will ask your reason for dropping out to determine if there are any adverse events that have not been reported.

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 flares and you require a large dose of Sandostatin to relieve your symptoms, in which case it would not be safe for you to continue. We would also end your participation if you became pregnant.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, or if you experience a research-related injury, please contact Dr. O'Dorisio at 319-356-3595**.**

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): _____

Do not sign this form if today's date is on or after EXPIRATION DATE: 09/14/18.

_____ _____

(Signature of Subject) (Date)

Parent/Guardian 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: 09/14/18.

_____	_____
(Signature of Parent/Guardian)	(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)