INFORMED CONSENT DOCUMENT

Project Title: **Comparator Study of 68Ga-DOTATOC PET/CT with Octreoscan + high-resolution, contrast-enhanced CT for diagnosis and staging in neuroendocrine tumors and other somatostatin receptor positive tumors**

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- 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 with special proteins called 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 see if it is as effective as having an Octreoscan and a diagnostic CT or MRI. Subjects 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. A "low dose" computed tomography (CT) scan will then be done on the same scanner. 68Ga-DOTATOC is considered investigational, which means that it has not yet been approved by the U.S. Food and Drug Administration (FDA). The FDA has granted permission to conduct this study under an investigator's new drug (IND) application.

We believe this special PET/CT scan will be able to see smaller tumors than the Octreoscan (indium [In-111] pentreotide) scan combined with a "high-dose, contrast-enhanced" CT scan or MRI that is the current standard of care.

HOW MANY PEOPLE WILL PARTICIPATE?

About 112 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 last up to 6 months and include 1 or 2 68Ga-DOTATOC PET/CT scans. You will have up to 5 visits, and 2 phone calls. The first 68Ga-DOTATOC PET/CT will be performed on your first or second visit and we will call you the next day to see how you feel or if you have had any reactions. You will come to UIHC or visit your local doctor between 1 and 7 days after the PET scan to have a blood test.

You have a second 68Ga-DOTATOC PET/CT scan 3-6 months later. This scan will require a visit during which you will have a physical exam, blood tests, and the second PET scan. We will call you the next day to see how you feel. You will come to UIHC or visit your local doctor between 1 and 7 days after the PET scan to have a blood test.

Each PET/CT scan will require that you spend 2-3 hours in the UIHC PET 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/CT 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?

- Visit One in Holden Comprehensive Cancer Center or Nuclear Medicine Department
  - Sign informed consent
  - Review pathology report with diagnosis of tumor
  - Review Octreoscan and high-resolution, contrast-enhanced CT or MRI
  - Have physical exam with vital signs (height, weight, blood pressure, heart rate, respirations, temperature)
  - Evaluate functional status using Karnofsky or Lansky scale
  - Have blood drawn for routine blood testing including a pregnancy test if you are of childbearing potential

- Visit Two in the PET Center (this visit may be combined with Visit One and occur on the same day as Visit One)
  - Record height, weight, blood pressure, heart rate, respirations, temperature
  - Have physical exam (not duplicated if Visit One is within 7 days)
  - Have blood drawn for routine blood testing including a pregnancy test if you are of childbearing potential (not duplicated if screening Visit One is within 7 days)
  - Have urine pregnancy test if you are of childbearing potential and Visit One was more than one day ago. We may give you a medicine, alprazolam (Xanax®) or lorazepam (Ativan®) 30 minutes before the PET scan to help you relax OR provide anesthesia/sedation if you are a child
  - Have an IV inserted
  - Receive IV injection of 68Ga-DOTATOC
  - Have PET/CT scan
  - Record blood pressure, heart rate, respirations
  - Remain in PET Center for observation for 2 hours after injection of 68Ga-DOTATOC as is standard for this type of procedure

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

- Visit Three in the Holden Comprehensive Cancer Center or with local physician (1-7 days after Visit Two)
  - Have blood drawn for routine blood testing.

- Visit Four in the PET Center (3-6 months after Visit Two assuming no disease progression)
    - Review your history of symptoms, biomarkers, any Octreoscan and high-resolution, contrast-enhanced CT or MRI, and any treatment received over past 6 months
    - Record weight, blood pressure, heart rate, respirations, temperature
    - Have blood drawn for routine blood testing including a blood pregnancy test if you are of childbearing potential)
    - We may give you a medicine, alprazolam (Xanax®) or lorazepam (Ativan®) 30 minutes before the PET scan to help you relax OR provide anesthesia/sedation if you are a child
    - Have an IV inserted
    - Receive IV injection of 68Ga-DOTATOC
    - Have PET/CT scan
    - Record blood pressure, heart rate, respirations
    - Remain in PET Center for observation for 2 hours after injection of 68Ga-DOTATOC as is standard for this type of procedure

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

- Visit Five in the Holden Comprehensive Cancer Center or with local physician (1-7 days after Visit Four)
    - Have blood drawn for routine blood testing.

  There is no long term follow-up for this study.

The PET/CT images for this study will be compared with your Octreoscan and high-resolution, contrast-enhanced CT or MRI's that are the current standard of care for your tumor. The images obtained for this study are being used to find medical abnormalities that might not be visible on the Octreoscan or high-resolution, contrast-enhanced CT or MRI. These images will be reviewed by a nuclear medicine physician and will be discussed with your doctors.

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, CT or MRI and an Octreoscan within the past 3 months, and what treatments you may have had since your last Octreoscan and CT or MRI.

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 risk of pain and/or infection at the site of your IV placement and in having blood drawn for the blood tests. If you elect to take Xanax or Ativan 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 hours after receiving Xanax or Ativan. You will need a driver to take you home or to your hotel if you take either of these two drugs. There may be a psychological risk associated with the scan detection more tumor than was previous known to be present by Octreoscan and high-contrast CT or MRI.

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. This does not include the radiation you received with your last Octreoscan and high-resolution, contrast-enhanced CT or MRI. Although there are no proven harmful effects from this amount of radiation, long term effects on your health such as cancer cannot be ruled out with certainty. 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, open on both ends, that which 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 15-35 minutes. You will be able to talk to people in the room through a speaker system. We will monitor you closely while you are inside the scanner. 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.

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 tell us if you may have become pregnant within the previous 14 days because the pregnancy test is unreliable during that time. 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.

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 6 months after your first, we may or may not be able to determine if your tumor has grown or if you have any new tumors.

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 or MRI for detecting somatostatin receptor positive tumors and identifying small tumors that might be missed by either Octreoscan or high-resolution, contrast-enhanced CT or MRI.

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 responsible for your travel costs.

Pregnancy tests, the cost of making and administering the 68Ga-DOTATOC, and the cost of the PET/CT, as well as the blood tests performed 1-7 days following the scan as required for participation in this trial, will be paid for by the study.

You and/or your medical/hospital insurance carrier will remain responsible for your regular medical care expenses, including any physical exams, blood chemistries, biomarker tests, Octreoscans or high-resolution, contrast-enhanced CTs or MRIs.

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) is 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. No one on the research team will receive a direct payment or increase in salary from NIH 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
- auditing departments of the University of Iowa
- 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 analyze the safety and effectiveness of the Ga-DOTATOC PET/CT in the diagnosis and staging 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 on the hard drive of a computer that can only be accessed with a special identification and password. The blood samples will be sent to the regular UIHC laboratory and the results will be put in your medical record. 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.

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. Once 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 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 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, 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://research.uiowa.edu/hso. 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: 02/02/16.**

_____ _____

(Signature of Subject) (Date)

FOR IRB USE ONLY
APPROVED BY: IRB-01
IRB ID #: 201212736
APPROVAL DATE: 02/20/15
EXPIRATION DATE: 02/02/16

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: 02/02/16.**

_____ _____

(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)