Patient Name: _____

DOB: ____ /_____ /_____

UCSF MRN: _____

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

CC# 17455: Yttrium-90 DOTA-TOC Intra-arterial (IA) Peptide Receptor Radionuclide Therapy (PRRT) for Neuroendocrine Tumor

WHAT IS THIS STUDY ABOUT?

This is a clinical trial, a type of research study. The study doctors, Dr. Thomas Hope and Dr. Emily Bergsland, or other participating doctors will explain the clinical trial to you.

Research studies include only people who choose to take part. Please take your time to make your decision about participating. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask your study doctor.

You are being asked to take part in this study because you have neuroendocrine tumor that expresses the somatostatin receptor. The majority of your disease is in your liver and your physician believes that liver-directed therapy can be beneficial, and your tumor is not considered surgically resectable. Recently, a new treatment option called Peptide Receptor Radionuclide Therapy (PRRT) has been shown to be effective in patients with neuroendocrine tumor. PRRT typically uses a drug called ^{177}Lu-DOTA-TATE. In this study, PRRT will be given using a different drug called ^{90}Y-DOTA-TOC. In addition to a different drug, this study involves a different route of administration. Rather than being infused through a vein in your arm (by IV), the drug will be infused directly into an artery in your liver (the hepatic artery) in order to increase the amount of drug that gets taken up by your liver tumors.

This informed consent form provides information about this study. Please read it carefully and ask any questions to your doctor. You are encouraged to discuss this with your family doctor and your family before taking your decision.

Once you understand the study and if you agree to participate, you will be asked to sign this informed consent form. You will be given a copy of the signed informed consent form to keep.

WHAT IS ^{90}Y-DOTA-TOC AND HOW IS IT USED?

^{90}Y-DOTA-TOC is a drug used for a type of treatment called Peptide Receptor Radionuclide Therapy (PRRT). PRRT is a targeted therapy that is performed by injecting a small molecule with a radioactive component, called a radionuclide, into the body. This molecule attaches to specific sites on tumor cells, called receptors, to kill the tumor cells. The radionuclide in ^{90}Y-DOTA-TOC, called Yttrium-90, delivers strong radiation directly into tumor cells. We hope that ^{90}Y-DOTA-TOC will work to focus the radiation to kill the tumors while having lesser side effects on healthy tissue. ^{90}Y-DOTA-TOC is not approved by the United States Food and Drug Administration (FDA), and is considered investigational.

This study will also look at the effects of giving ^{90}Y-DOTA-TOC directly into the liver (hepatic artery), instead of into a vein in your arm. By injecting the drug directly into the liver, the drug will enter the liver before going to the rest of the body. We hope that this will allow more of the drug to reach and attack the liver tumor while decreasing toxicity and harmful effects. Although the ^{90}Y-DOTA-TOC will be administered into the liver, it will also go throughout your body, possibly collecting in, and treating, areas of tumor outside of the liver.

When ^{90}Y-DOTA-TOC is used, it is typically administered by IV (through a vein) at a dose of 75-120 mCi, given 2-4 times. In this study, ^{90}Y-DOTA-TOC will be given <u>one time</u>, at a dose of 80-115 mCi. The dose of ^{90}Y-DOTA-TOC used in this study is less than the dose that is used when ^{90}Y-DOTA-TOC is given by IV. There will not be any repeat administrations of ^{90}Y-DOTA-TOC. We believe that one administration of ^{90}Y-DOTA-TOC, delivered directly to the liver rather than through a vein, will have an anti-cancer effect.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to determine if injecting ^{90}Y-DOTA-TOC directly into the liver is safe and reduces the size of liver tumors in patients with somatostatin receptor positive neuroendocrine tumors.

This study is funded by the Neuroendocrine Tumor Research Foundation, the North American Neuroendocrine Tumor Society, and the UCSF Medical Center Strategic Initiative Funding Program.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

About 32 people will participate in this study at UCSF.

WHAT WILL HAPPEN TO ME IF I TAKE PART IN THIS RESEARCH STUDY?

Before you begin the study...

To find out if you can be in the study, the following procedures will be done within 4 weeks of receiving the study drug:

- **Medical chart review:** Your medical chart will be reviewed by the study doctors. The history of your tumor will be reviewed.
- **Physical Exam and vital signs:** A physical exam will be performed including a review of your medical history. Your blood pressure, heart rate and temperature will also be taken.
- **Blood tests**: Your medical chart will be reviewed for recent laboratory values. If needed, your blood will be drawn by sticking a needle into a vein in your arm. These blood samples will be used to test for hematological, liver and kidney function tests.
- **Pregnancy testing (for women of child bearing potential)**: Because the drugs in this study can affect a fetus, pregnant women may not participate in this study. If you are a woman of child bearing potential, a urine or blood test will be done to make sure you are not pregnant.
- **Liver imaging**: You will have an MRI imaging study of your liver within 28 days of your treatment. If you cannot have an MRI, a CT of the abdomen will be performed.
    - A **CT** scan uses special x-ray equipment to make detailed pictures of body tissues and organs. For this exam, you will need to lie still on a table inside a large doughnut-shaped machine. The table will move and the machine will make clicking and whirring noises as the pictures are taken. If necessary, an iodine dye (contrast material) will first be given. The iodine dye makes tissue and organs more visible in the pictures. The iodine dye may be given orally (by mouth), intravenously (into a vein), or rectally (fill up the loops of your bowels). The CT scan is done in the radiology department and takes about 30 minutes.
    - An **MRI** uses special equipment to make detailed pictures of body tissues and organs. For this exam, you will lie down on a narrow bed which will then be placed in a tunnel that is 6 feet long by 2 feet wide and open at each end. You will need to lie there quietly for about one hour, during which there will be a loud banging noise. You may feel warm during this procedure. If necessary, gadolinium (contrast material) will first be injected into a vein. The gadolinium makes tissue and organs more visible in the MRI. The MRI scan is done in the radiology department and takes about 90 minutes.

- **Somatostatin receptor PET scan:** You will have a somatostatin receptor PET/CT or PET/MRI scan done to show that your neuroendocrine tumor has somatostatin receptors. Only patients with tumors that have somatostatin receptors can participate in this study. This scan will be done using a somatostatin receptor imaging agent called ^{68}Ga-DOTA-TOC. A PET scan is a special type of test to show how the organs and cells work in your body and is done to show activity of the cells in your tumor. Your PET scan will begin with an injection of a radioactive substance into a vein in your arm. You will be asked to rest quietly for a period of time (about 60 minutes) as the radioactive substance circulates throughout your body. After this time, you will be positioned within a large ring (similar to being in the center of a big donut) on a scanning bed. Once positioned properly, the bed will move you into the scanner. As pictures are being taken, you will be asked to remain very still so clear images will be taken. The imaging time takes about one hour.

During the main part of this study…

If the screening procedures show that you can continue to be in the study, and you choose to take part, then you will receive a single dose of ^{90}Y-DOTA-TOC and be followed for six months, or until your disease progresses.

The following tests and procedures will be done during the main part of the study. All study procedures will be done at Mission Bay Hospital in San Francisco, California.

PRRT procedure using ^{90}Y-DOTA-TOC

You will be given sedation for this procedure and may not eat or drink anything after midnight the evening before your procedure. This procedure will take approximately 4 hours.

- **Blood draw:** You will have your blood drawn the morning of the procedure to make sure it is okay for you to receive the study drug.
- **Angiogram**: The first part of the treatment procedure is called an angiogram, and involves putting a thin long tube called a catheter into the artery in your groin and guiding it using low dose X-rays to the artery supplying blood the liver. Then, the catheter is moved into the vessel that is supplying blood to the tumors.
    - **^{90}Y-DOTA-TOC Infusion**: Once the catheter is in the correct position, you will receive ^{90}Y-DOTA-TOC through an artery in your liver. Vital signs (blood pressure, heart rate and temperature) will be taken prior to, during, and after injection.
    - **Amino Acid Infusion**: You will receive a four-hour infusion of amino acids to protect your kidneys from radiation associated with the ^{90}Y-DOTA-TOC infusion. The amino acid infusion will be done during the entire length of the PRRT procedure.

Several people will be present during the procedure in order to make sure the drug is administered safely, including several doctors, a nurse, a radiology technologist, and radiation safety officer. UCSF Radiation Safety will speak to you before your procedure to determine if you need to be admitted to the hospital in order to minimize exposure to the public. If you are travelling a significant distance and cannot return home the night of the treatment, it is likely that you will stay in the hospital the night of the procedure rather than a hotel. A written handout with radiation safety instructions will be given to you after the procedure.

You should not lift anything heavier than 10 pounds for 3 days after the procedure to make sure that you don't develop bleeding in the groin. The radiation released by the drug will stay in your body for about 12 days. If you have any serious problems or complications after treatment, you should contact the study doctor immediately, and you may be admitted to the hospital for observation and management of the problem.

Post-PRRT radiation precautions: Your body will give off radiation following therapy for a certain period of time, depending on how quickly your kidneys clear the drug from your body, so there are a number of precautions you will have to follow after the procedure to minimize radiation exposure to others. Toilets should be used in a seated position, and you should wash your hands after using the toilets. For two days after the procedure, please drink enough water that you use the toilet at least every hour. You should keep at least 3 feet from people you live with for 2-3 days after treatment. For seven days you should sleep in separate beds from your partner and sexual activity is not recommended. Please shower daily for seven days. Both men and women should abstain from procreation for six months after the final administration and use contraception. Please bag any items that contain body fluids that cannot be flushed down the toilet (menstrual pads and pajamas).

Follow-up

- **Blood draws:** you will have your blood drawn 1, 4, 12, and 24 weeks after treatment to check for toxicities.
    - **Additional follow-up:** The first 10 patients participating will also have bloodwork and a follow-up telephone call 8 weeks after the PRRT procedure.
- **Imaging:** you will have **CT** or **MRI** scan of your liver at 12 and 24 weeks after treatment.
- **Office visits:** you will be asked to follow up in the office 1, 4, 12 and 24 weeks after treatment. During each office visit you will have a physical exam and the study doctor will ask about your medical history and how well you are able to do daily activities

HOW LONG WILL I BE IN THE STUDY?

Participating in this study will take about 7 months and you will follow-up with the study team once a year after that (in clinic or by telephone), unless you decide to withdraw your consent for participation in this study. Withdrawing your consent to participate in this study will not affect your medical care/treatment whatsoever, and your doctor will continue to follow you as a patient. You can stop taking part in this study at any time. If you decide to stop taking part in the study, we encourage you to talk to your medical team first.

CAN I STOP BEING IN THE STUDY?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop your participation safely. The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

WHAT SIDE EFFECTS OR RISKS CAN I EXPECT FROM BEING IN THE STUDY?

You may have side effects while on the study. Side effects may be mild or serious. Your study team may give you medicines to help lessen side effects. You should talk to your study doctor about any side effects you experience while taking part in the study. There also is a risk of death.

Risks of Treatment with ^{90}Y-DOTA-TOC (rates are estimates)
The risks of ^{90}Y-DOTA-TOC listed below are based on studies where patients with neuroendocrine tumor were given ^{90}Y-DOTA-TOC or PRRT through a vein (by IV). In this study, ^{90}Y-DOTA-TOC will not be given by IV – it will be administered directly into the liver. Because ^{90}Y-DOTA-TOC is given differently in this study, the likelihood that you will experience these risks may differ from the rates (percentages) listed below.

<u>Likely</u>

- Nausea (59%)
- Vomiting (47%)
- Tiredness (40%)
- Abdominal pain (29%)

<u>Less likely</u>

- Bone marrow injury (anemias) (14%; 51 out of 360 patients given IV ^{90}Y-DOTA-TOC)

Rare but serious

- Kidney damage (less than 3%; 10 out of 358 patients given IV ^{90}Y-DOTA-TOC)
- Secondary malignancies such as leukemia (less than 2%; 8 out of 807 patients given IV PRRT)
- Liver damage (rates not reported)
- Death (rates not reported)

One patient at UCSF experienced a blood clot in the lung and abdominal pain after receiving Yttrium-90 DOTA-TOC. These adverse events could be related to the patient's disease, but a relationship to Yttrium-90 DOTA-TOC cannot be ruled out.

Risks and side effects related to study drug ^{90}Y-DOTA-TOC:

- **Radiation risk summary**: This research study involves exposure to a significant amount of radiation. Most of the radiation is from the therapy to treat your medical condition. The target of this radiation is the tumor, however, for each therapy, other organs are exposed as follows: Spleen (19 Gy), kidneys (11 Gy), bladder (7 Gy) liver (3 Gy), red Marrow (0.3 Gy). While this amount of radiation is intended to treat your condition, it does involve a risk of a secondary cancer. However, the UCSF Radiation Safety Committee has reviewed the use of radiation in this research study and has designated this use as acceptable to obtain the benefits provided by the results of the study. If you are pregnant or breast feeding, you SHOULD NOT participate in this study. If you have any questions regarding the use of radiation or the risks involved, please consult the physician conducting the study.
    - **Bone marrow effects**: Radiation can kill bone marrow cells that can lead to low levels of red blood cells, platelets (a special cell which helps the blood to clot), and other blood cells such as white blood cells (helps to fight infection). A decrease in the various blood cell types may put you at risk for bleeding, fatigue, shortness of breath, and infection. This happens in many patients and is frequently temporary. Your blood counts will be checked after the treatment to make sure you have not developed significant bone marrow injury.
    - **Renal (kidney) effects**: ^{90}Y-DOTA-TOC is cleared from the body through the kidneys, which results in high levels of radiation exposure to the kidneys. This increases the chance that you may develop transient or chronic kidney injury. You will receive an infusion throughout the administration of the ^{90}Y-DOTA-TOC that contains amino acids. This fluid is given in order to minimize the dose to your kidneys. Your kidney function will be checked to make sure you have not developed significant kidney injury.

  - **Liver effects**: Liver toxicity is not considered a significant risk associated with 90Y-DOTA-TOC treatment when given through a vein in the arm. In the patients reported receiving intra-arterial doses there have not been reports of liver toxicity, but the number of patients treated has been small. It is possible that there will be liver toxicity associated with the treatment and you will be followed after treatment to see if there was any injury to your liver.
  - **Secondary cancers**: The high dose of radiation associated with this therapy increases the risk of developing cancers later in your life. In particular, hematopoietic malignancies (such as leukemia) are at increased risk, although rare.
- **Gastrointestinal disorders**: You may experience nausea, vomiting and abdominal pain during the therapy. These usually resolve within the first day of therapy. You will be given medications to minimize the nausea and vomiting associate with the study drug. Patients may have frequent nausea and decreased appetite lasting up to one week after treatment.
- **Pregnancy and birth control**: The risks of ^{90}Y-DOTA-TOC to pregnant women and to unborn baby are unknown. But since ^{90}Y-DOTA-TOC is a radioactive drug, it has the potential to harm a developing fetus. Therefore, patients of childbearing potential must use an effective form of birth control during their participation in this protocol and for a minimum of 6 months after ^{90}Y-DOTA-TOC administration. You should discuss your birth control methods with the doctor to make sure it is considered appropriate (such as birth control pills, injections, or barrier methods). You cannot take part in this protocol if you are pregnant or breastfeeding. If you are a woman who is of childbearing potential, you will be given a pregnancy test before you begin this study to test for pregnancy. If you become pregnant during the study, you must notify your doctor immediately so all appropriate measures can be taken including but not limited to stopping participation and closely monitoring the pregnancy.

<u>Risks related to study procedures</u>:

- **Risks related to IV insertions and blood draws**: The placement of a venous catheter is associated with temporary discomfort from the needle stick, bruising, infection, and fainting.
- **Risks of Catheter Placement (during ^{90}Y-DOTA-TOC administration):** Possible side effects include pain at the insertion site, clotting or tearing of an artery, or bleeding at the catheter insertion site.

- **Risks of Imaging studies**:
    - **PET scan risks:** The PET scan involves exposure to radiation. The radiation exposure comes from a tracer which is a radioactive chemical injected into a vein in your arm. The tracer lets the doctor see how your cells are functioning. As with all injections, it may feel like a small sting and there may be possible bruising at the injection site. For some patients, having to lie still on the scanning table for the length of the procedure may cause some discomfort or pain. The radioactive solution does not remain in your system for a long period of time. See Radiation Risk.
    - **CT scan risks:** CT scans involve the risks of radiation, although much lower doses than associated with the ^{90}Y-DOTA-TOC. In addition, if contrast material (iodine dye) is used, there is a slight risk of developing an allergic reaction, from mild (itching, rash) to severe (difficulty breathing, shock, or rarely, death). The contrast material may also cause kidney problems, especially if you are dehydrated or have poor kidney function. The study doctors will ask you about any allergies or related conditions before the procedure. If you have any of these problems, you may not be allowed to have a CT scan. Having a CT scan may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia when placed inside the CT scanner, or by lying in one position for a long time. If contrast material is used, you may feel discomfort when it is injected. You may feel warm and flushed and get a metallic taste in your mouth. Rarely, the contrast material may cause nausea, vomiting or a headache.
    - **MRI risks:** Because the MRI machine acts like a large magnet, it could move iron-containing objects in the MRI room during your examination, which in the process could possibly harm you. Precautions have been taken to prevent such an event from happening; loose metal objects, like pocket knives or key chains, are not allowed in the MRI room. If you have a piece of metal in your body, such as a fragment in your eye, aneurysm clips, ear implants, spinal nerve stimulators, or a pacemaker, you will not be allowed into the MRI room and cannot have an MRI. Having an MRI may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia and by the loud banging noise during the study. Temporary hearing loss has been reported from this loud noise. This is why you will be asked to wear earplugs. At times during the test, you may be asked to not swallow for a while, which can be uncomfortable.

- **Procedure Delay**: Rarely the synthesis of the Y90 DOTATOC is not successful. This will not be known until the day of the procedure, so the procedure may be cancelled the morning of the procedure if synthesis failure occurs.
- **Unknown Risks:** The experimental treatments may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

For more information about risks and side effects, ask your study doctor.

ARE THERE BENEFITS TO BEING IN THE STUDY?

It is possible that ^{90}Y-DOTA-TOC may stop the tumor from getting worse. There is some evidence to suggest that this type of tumor may respond to the study drug. How a tumor responds to ^{90}Y-DOTA-TOC can be different from one patient to another. Sometimes the tumor can get smaller although it may still be present; there is a possibility that the tumor might disappear. In some cases, the tumor does not get any smaller but stops growing, and in some cases the tumor might even grow. The drug could also reduce the amount of symptoms that you experience from the tumor.

It is also possible that you may not benefit at all from participating in this study.

WHAT OTHER CHOICES DO I HAVE IF I DO NOT TAKE PART IN THIS STUDY?

There are a number of drugs approved for different neuroendocrine tumors including somatostatin analogues, everolimus and sunitinib. In addition to drugs, there are other liver targeted therapies that are used to treat patients with neuroendocrine tumors including trans-arterial chemoembolization and radiofrequency ablation. You may ask your doctor for all information you may be interested in. If you want to withdraw from the study, you can be treated with alternative drugs at any time. Please talk to your doctor about these options.

WILL MY MEDICAL INFORMATION BE KEPT PRIVATE?

Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total privacy. Some information from your medical records will be collected and used for this study. If you do not have a UCSF medical record, one will be created for you. Your signed consent form and some of your research tests will be added to your UCSF medical record. Therefore, people involved with your future care and insurance may become aware of your participation and of any information added to your medical record as a result of your participation. Study tests that are performed by research labs, and information gathered directly from you by the researchers will be part of your research records but will not be added to your medical record. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The University of California
- The National Cancer Institute (NCI) and other governmental agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

The drug product (^{90}Y-DOTA-TOC) and the additional imaging as part of the optional imaging sub-study will be provided at no cost to you.

Two types of procedures will be done during this study. Some are part of your standard medical care and others are only for research. You or your insurer will be billed for the standard medical care. You will be responsible for your co-pays, deductibles, and any other charges that your insurer will not pay. There is a possibility that your insurer may not cover standard medical care costs because you are in a research study or because you are receiving medical services out of network.

Before you agree to be in this study, you may want to contact your healthcare payer/insurer to see if your plan will cover the costs required as part of your participation. You may request more information about the costs of participating in this study and discuss this with the study team.

If you have any questions, your doctor and the study team will be able to provide you with answers.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://cancer.gov/clinicaltrials/understanding/insurance-coverage. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call **1-800-4-CANCER (1-800-422-6237)** and ask them to send you a free copy.

WILL I BE PAID FOR TAKING PART IN THIS STUDY?

You will not be paid for taking part in this study.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?

It is important that you tell your study doctor, Dr. Thomas Hope, if you feel that you have been injured because of taking part in this study. You can contact your study doctor in person or by phone at [redacted] or email [redacted].

Treatment and Compensation for Injury: If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California, depending on a number of factors. The University does not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Institutional Review Board at 415-476-1814.

WHAT ARE MY RIGHTS IF I TAKE PART IN THIS STUDY?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?

You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor, Dr. Thomas Hope or his research associates, at [redacted] or by email [redacted].

For questions about your rights while taking part in this study, call the UCSF Institutional Review Board (a group of people who review the research to protect your rights) at (415) 476-1814.

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ADDITIONAL IMAGING SUB-STUDY SECTION (*first 15 patients*):

The main study described above also has a related additional sub-study, which includes additional imaging procedures. The additional imaging will be used to look at whether giving the study drug directly into the liver allows more drug to reach the tumor, when compared with administering the drug into a vein in the arm.

The first 15 study participants eligible for the sub-study will be required to take part and have additional imaging procedures. If you are participating in this sub-study, you will receive:

1) **Additional 68Ga-DOTA-TOC administration and imaging on the day of the PRRT procedure. The procedures you receive will depend on when you enroll in the study – your study doctor can tell you what procedures you will have if you decide to participate in this study and sub-study.**

- **Participants 1-5 and 11-15:** During the PRRT procedure, a small amount of ^{68}Ga-DOTA-TOC will also be administered with the ^{90}Y-DOTA-TOC. ^{68}Ga-DOTA-TOC is the imaging agent used for the somatostatin receptor PET scan. After the completion of the arterial administration, a PET/CT scan will be done to look at the distribution of ^{68}Ga-DOTA-TOC injected into the liver.
    - A **PET/CT** scan shows how the organs and cells work in your body and is done to show activity of the cells in your tumor. You will be asked to not eat for six hours before the scan and to drink at least two large glasses of water within one hour of the study. Your PET scan will begin with an injection of a radioactive substance into a vein in your arm. You will be asked to rest quietly for a period of time (usually about 20 to 40 minutes) as the radioactive substance circulates throughout your body. After this time, you will be positioned within a large ring (similar to a big donut hole) on a scanning bed. Once positioned properly, the bed will move you into the scanner. As pictures are being taken, you will be asked to remain very still so clear images will be taken. The imaging time takes about one hour.
- **Participants 6-10:** Prior to the PRRT procedure, a small amount of ^{68}Ga-DOTA-TOC will be given through a vein in your arm. ^{68}Ga-DOTA-TOC is the imaging agent used for the somatostatin receptor PET scan. Six hours after the doctors begin administering ^{90}Y-DOTA-TOC, before you are discharged, a SPECT/CT scan will be done to look at the distribution of ^{68}Ga-DOTA-TOC injected into the liver.
    - A **SPECT/CT** scan shows the injected activity of the 90Y-DOTA-TOC in the cells of your tumor. You will be positioned within a large ring (similar to a big donut hole) on a scanning bed. Once positioned properly, the bed will move you into the scanner. As pictures are being taken, you will be asked to remain very still. The imaging takes about one hour.

2) A PET/MRI the day after the PRRT procedure

- The day after treatment, all patients in the sub-study will have a PET/MRI done, as long as it is safe to do so. There will be no additional administrations. This scan will be used to see where the 90Y-DOTA-TOC went in the liver.
  - An **MRI** uses special equipment to make detailed pictures of body tissues and organs. For this exam, you will lie down on a narrow bed which will then be placed in a tunnel that is 6 feet long by 2 feet wide and open at each end. You will need to lie there quietly for about one hour, during which there will be a loud banging noise. You may feel warm during this procedure. If necessary, gadolinium (contrast material) will first be injected into a vein. The gadolinium makes tissue and organs more visible in the MRI. The MRI scan is done in the radiology department and takes about 90 minutes.

Benefits

The imaging sub-study is not designed specifically to help you. It might help to demonstrate whether injecting the study drug directly into the liver allows more drug to reach the tumor, when compared with administering the drug through a vein in your arm.

Risks related to additional imaging

- **Radiation risks:** Additional imaging performed as part of this sub-study involve exposure to radiation. The additional amount of radiation that you will receive as a result of participating in this sub-study will be a maximum of approximately 4.5 mSv. This is equivalent to 1.5 times the yearly natural background of radiation in the US (3 mSv). This amount of radiation is in addition to the radiation exposure related to the procedures performed during the main study. This amount of radiation involves a low risk of cancer. However, the UCSF Radiation Safety Committee has reviewed the use of radiation in this research study and has designated this use as acceptable to obtain the benefits provided by the results of the study. If you are pregnant or breast feeding, you SHOULD NOT participate in this study. If you have any questions regarding the use of radiation or the risks involved, please consult the physician conducting the study.
- **PET scan risks:** The PET scan involves exposure to radiation. The radiation exposure comes from a tracer which is a radioactive chemical injected into a vein in your arm. The tracer lets the doctor see how your cells are functioning. As with all injections, it may feel like a small sting and there may be possible bruising at the injection site. For some patients, having to lie still on the scanning table for the length of the procedure may cause some discomfort or pain. The radioactive solution does not remain in your system for a long period of time. See Radiation Risk.

- **CT scan risks:** CT scans involve the risks of radiation, although much lower doses than associated with the ^{90}Y-DOTA-TOC. In addition, if contrast material (iodine dye) is used, there is a slight risk of developing an allergic reaction, from mild (itching, rash) to severe (difficulty breathing, shock, or rarely, death). The contrast material may also cause kidney problems, especially if you are dehydrated or have poor kidney function. The study doctors will ask you about any allergies or related conditions before the procedure. If you have any of these problems, you may not be allowed to have a CT scan. Having a CT scan may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia when placed inside the CT scanner, or by lying in one position for a long time. If contrast material is used, you may feel discomfort when it is injected. You may feel warm and flushed and get a metallic taste in your mouth. Rarely, the contrast material may cause nausea, vomiting or a headache.
- **MRI risks:** Because the MRI machine acts like a large magnet, it could move iron-containing objects in the MRI room during your examination, which in the process could possibly harm you. Precautions have been taken to prevent such an event from happening; loose metal objects, like pocket knives or key chains, are not allowed in the MRI room. If you have a piece of metal in your body, such as a fragment in your eye, aneurysm clips, ear implants, spinal nerve stimulators, or a pacemaker, you will not be allowed into the MRI room and cannot have an MRI. Having an MRI may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia and by the loud banging noise during the study. Temporary hearing loss has been reported from this loud noise. This is why you will be asked to wear earplugs. At times during the test, you may be asked to not swallow for a while, which can be uncomfortable.

CONSENT

You have been given copies of this consent form and the Experimental Subject's Bill of Rights to keep. You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

If you wish to participate in this study, you should sign below.

Date	Participant's Signature for Consent
Date	Person Obtaining Consent
Date	Witness Signature (Only required if the participant is a non-English speaker)