Targeted Dual Modality Imaging (TDMI) for Detection and Removal of Head and Neck Cancer Radiation

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Study Title: **Targeted Dual Modality Imaging (TDMI) for Detection and Removal of Head and Neck Cancer**
Version Date: **01/16/2025**
PI: **Eben Rosenthal**

Name of participant: _____ Age: _____

The following is given to you to tell you about this research study. Please read this form with care and ask any questions you may have about this study. Your questions will be answered. Also, you will be given a copy of this consent form.

Key Information:
The first section of this document contains some key points that the research team thought you would find important. The study is described in more detail after this section. If you do not understand something, please ask someone.

Key information about this study:

General Information	You are invited to take part in a research study. This research study is voluntary, meaning you do not have to take part in it. The procedures, risks, and benefits are fully described further in the consent form.
Purpose	The purpose of the study is to determine the distribute pattern of ^{111}In panitumumab and panitumumab-IRDye800 in patients with head and neck squamous cell carcinoma (HNSCC) that will undergo head and neck cancer surgery.
Duration & Visits	Your participation in this research study is expected to take approximately 45 days, with up to 30 days for screening to see if you are eligible to participate (screening period can be shorter than 30 days) and approximately 15 days on study. You will only have 2 research specific visits, in addition to your normal pre-operative, surgery and follow up clinic visits and examinations.
Overview of Procedures	If you agree to enroll, you will receive a one-time infusion of panitumumab-IRDye800 and injection of ^{111}In panitumumab, then following one SPECT/CT scan 1 -7 days before your surgery to remove your cancer. You will be evaluated for any reactions to the drug immediately after the injection, before your surgery, and up to 15 days after your surgery.

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Risks	The most likely risks are infusion reactions, rash, dry or itchy skin, fatigue, decreased magnesium and/or other minerals in your blood, and a small amount of radiation exposure.
Benefits	You may or may not have a direct benefit from being in the study. But the study doctors hope to be able to use the information on the safety of the study drug to help treat future cancer patients.
Alternatives	You should not feel obligated to agree to participate. Your questions should be answered clearly and to your satisfaction. If you decide not to participate, please tell the Protocol Director.

Detailed Information:
The rest of this document includes detailed information about this study (in addition to the information listed above).

You are being asked to take part in this research study because you have been diagnosed with HNSCC and plan to undergo surgery with curative intent, meaning the intent of your planned surgery is to remove all of cancer if possible. This involves not only taking out the tumor itself, but also finding the lymph nodes that may have received cancerous cells (metastases) from your primary tumor. At our site, we are looking to enroll approximately 40 participants.

You do not have to be in this research study. You may choose not to be in this study and get other treatments without changing your healthcare, services, or other rights. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study. Your medical record will contain a note saying you are in a research study and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

Side effects and risks that you can expect if you take part in this study:
There are risks, discomforts, and inconveniences associated with any research study. These deserve careful thought. You should talk with the Protocol Director if you have any questions.

Potential Risks of Panitumumab (VECTIBIX ®)
^{111}In panitumumab and panitumumab-IRDye800 contain the panitumumab antibody. Panitumumab is approved by the US FDA for treatment of certain types of advanced colorectal cancer at a dosage of 6 mg/kg given every 14 days. Many of the reported adverse events are

associated with repeat administration of panitumumab, rather than the single dose that you will receive as part of this study. The total dose of panitumumab that you will receive will be lower than the usual total dose that is given to patients receiving it as treatment for cancer.

The most common side effects patients have experienced when receiving panitumumab primarily include skin reactions (including acne like rash, dry or itchy skin, cracking of skin around your nail beds, skin infections, and dry eyes), fatigue, nausea, and diarrhea. Monitor skin reactions carefully to prevent serious or life-threatening complications. Exposure to sunlight may make skin reactions worse; limit exposure by using sunscreen and protective clothing.

Infusion reactions, including fever, chills, difficulty or labored breathing, and low blood pressure, occurred in 4% of patients taking panitumumab. These reactions are most likely during or immediately following panitumumab infusion. Severe infusion reactions occurred in 1% of patients. Based on your study doctor's routine practice, he or she may decide to give other drugs, such as an antihistamine called diphenhydramine (Benadryl) or steroids, if it's felt necessary to treat a reaction**. Tell your doctor or nurse immediately if you experience any of the symptoms of an infusion reaction.**

Patients receiving repeated doses of panitumumab occasionally had progressively decreased magnesium and/or other minerals in the blood. Your blood chemistry levels will be monitored closely during this study, and electrolyte replacement will be given if necessary.

There have been rare reports of patients experiencing fatal and non-fatal lung disease after treatment with panitumumab. You should notify your study doctor if you have ever had lung disease. Notify your study doctor immediately if you experience sudden or worsening breathing troubles.

Potential Risks of ^{111}In panitumumab
The expected risks of ^{111}In panitumumab are expected to be the same as the known risks of panitumumab (see above section) and the additional risks of the ^{111}In chelator, diethylenetriamine pentaacetate (DTPA).

We use DTPA to help us link together panitumumab and Indium, as a result DTPA is found in the solution containing the study agent, ^{111}In panitumumab.

We do not believe that the study drug will increase your chances of experiencing known side effects from treatment with panitumumab; however, we do not know this for sure. The most common dose independent side effects associated with panitumumab are infusion reaction or allergic reactions, described in the panitumumab risk section above. ^{111}In panitumumab is

radioactive, so you will be exposed to a small amount of radiation from the study drug. The radiation risks are discussed in a separate section below.

Potential Risks of Zinc/Calcium Diethylenetriamine Pentaacetate (DTPA)
DTPA (Diethylenetriamine pentaacetate) is an FDA approved medicine that can bind to radioactive metals to decrease the amount of time it takes to get out of the body.

Common side effects of Ca DTPA include

- headache
- lightheadedness, feeling of going faint.
- chest pain
- allergic reaction
- skin inflammation
- metallic taste
- nausea
- diarrhea
- injection site reactions, and
- loss of certain essential nutritional metals (such as zinc, magnesium, and manganese) from the body.

Radiation Risks:

You are agreeing to participate in a research project that involves the use of imaging procedures that expose you to radiation. This section will discuss the risks associated with the imaging procedures that are for research only. Your doctors may order additional imaging procedures as part of your normal patient care that also expose you to radiation. Those normal imaging procedures are not included in the risk discussion below. Please discuss those procedures and radiation risks with your doctors. As part of this research study, you may be asked to have a SPECT/CT (Single-Photon Emission Tomography-Computed Tomography) imaging procedure that exposes you to radiation. Most of the exposure comes from the injected radioactive imaging agent. The amount of radiation that you could receive is approximately 84% of the amount allowed annually for persons exposed to radiation as part of their work. Additionally, to protect your bladder from the effects of the injected radioactive substance, you should drink plenty of fluids and empty your bladder every two hours for at least the first six hours after you have the SPECT/CT scan.

Potential Reproductive Risks
Women of Childbearing Potential

Based on data from animal studies, panitumumab may cause fetal harm (organ damage, death) when administered to pregnant women. If you are a woman who is able to become pregnant, it is expected that you will use an effective method of birth control to prevent exposing a fetus to a potentially dangerous agent with unknown risk. If you are pregnant or currently breast feeding, you may not participate in this study. You understand that if you are pregnant, if you become pregnant, or if you are breast feeding during this study, you or your child may be exposed to an unknown risk.

Potential Study Procedure Risks
Blood Draw/IV: Inserting a needle into your arm for drawing blood, or an IV catheter for infusion, can cause slight discomfort or bruising at the puncture site. Lightheadedness or fainting may occur. Rarely, an infection at the puncture site may occur.

ECG: The adhesive pads used during this procedure may cause mild skin irritation or pull out some hairs when removed.

Risks that are not known:
Because this study is investigational, meaning non-FDA approved, there may be risks that we do not know about at this time.

Good effects that might result from this study:
The benefits to science and humankind that might result from this study:
You may not benefit directly from taking part in this study. However, information obtained from your participation in this study may benefit other people with cancer in the future and help evaluate detection of subclinical disease during primary tumor removal using systemic administrations of both ^{111}In panitumumab and panitumumab-IRDye800 prior to surgery compared to standard of care procedures for tumor detection.

We cannot and do not guarantee or promise that you will receive any benefits from this study.

Procedures to be followed:
If you choose to participate in this study, Dr. Eben Rosenthal and his research team will perform the procedures listed below in addition to your normal pre-operative, surgery and follow up clinic visits and examinations.

Please refer to **Table 1: Study Calendar for all visit specific procedures.**

Screening Period
If you choose to participate in the study and sign this consent form, you will have to undergo the following exams and tests to determine if you are eligible to take part in this study**. If you have already had some of these exams and tests recently, they may not need to be repeated.** The screening period will not last more than 30 days.

The following procedures will occur during screening:
- Review your medical history and current medications.
- Physical exam, including height, weight, and vital signs (blood pressure, heart rate, respiratory rate, and temperature).
- Performance status – a measure of how you are feeling.
- Electrocardiogram (ECG) – a test to measure and record the electrical activity of your heart. Sticky pads will be placed at different points on your body and you will be asked to lie still while the machine records your heart activity.
- Blood draw for lab safety tests (approximately 2 teaspoons).
- Pregnancy test (approximately ½ teaspoon of blood): If you are a woman who could have children, please ensure to use effective contraception during screening and to be continued for 2 months following administration of panitumumab-IRDye800 and ^{111}In-panitumumab doses. If you are pregnant or breast feeding you cannot participate in this study because of the potential unknown risk to your unborn fetus or baby.
- Assessment for concomitant medications.
- Assessment of adverse events.
- Obtain a copy of results from an ^{18}F FDG PET/CT or ^{18}F FDG PET/MRI scan that was part of your standard of care pre-operative tests.

Day 0
If you meet all the requirements to participate, you will come to clinic on Day 0 to receive the investigational imaging agents. The following procedures will occur:

<u>Prior to administration of Study Agent</u>
- Urine pregnancy test for women of childbearing potential. Please ensure to use effective contraception for 2 months following administration of panitumumab-IRDye800 and ^{111}In-panitumumab doses.
- Record vital signs.
- ECG
- Review any current medications.

Administration of panitumumab-IRDye800: The agent will be given as a single dose over 15 minutes through an IV tube into a vein in your arm. You will be observed for 30 minutes following completion of the infusion, and ECG, vistal signs will be recorded

Administration of ^{111}In panitumumab: The study agent will be given as a single dose as a bolus injected into a vein in your arm.

Observation (30 minutes): Safety monitoring for 30 minutes after the end of the study agent administration to watch for side effects. Your study doctor may prescribe other medications to treat or prevent side effects. At any time during this treatment, it is important for you to let your doctor or nurse know if you experience anything that does not feel normal.

- Record any side effects or medications given, at end of 30 minutes observation period.

Day 1 to Day of Surgery

On Day 1 to Day of Surgery, depending on schedule availability, you will come to clinic to have ^{111}In panitumumab SPECT/CT imaging. The following procedures will occur:

- SPECT/CT imaging: During image collection, study doctors will collect both SPECT images, which detect the small amount of radiolabeled ^{111}In panitumumab imaging agent, and CT images, which uses X rays, to look at your tissues and organs. You will be asked to lie on a long narrow couch for about 20 minutes while the machine gathers data.
- Record any side effects and review current medications.

Day of Surgery

On the day of surgery, the following procedures will occur:

- Surgical imaging and resection of cancer tissue – You will have the same surgery you would receive if you were not part of a research study. The details of this surgery will be part of your regular medical care and will be determined by your surgeon based on your medical condition.
  - The surgeon will inject an optical dye per surgeon preference, which is a standard procedure for sentinel node mapping.
  - Prior to, and once the surgeon has removed as much cancer as per the surgical plan using standard methods, the investigator will use additional special cameras (fluorescence cameras) to take extra images of the tumor for the study.
  - Prior to, and once the surgeon has removed the lymph nodes from the neck per the surgical plan using standard methods, the investigator will use additional special cameras (fluorescence cameras) and gamma probe to take extra images and measurements of the lymph nodes for the study.
- Pathology evaluations – after removal, tumor and lymph node tissues will be sent to the pathology laboratory as standard practice.

The research imaging and evaluations will not affect the routine diagnostic pathology tests that will be performed on your tissues.

Day 15
You will be asked to return to clinic and the following procedures will occur:

- Clinical assessment performed in-person, via telehealth, or chart review to include collection of any additional adverse events that are attributable to the study and/or concomitant medications.
- ECG only if indicated.

Table 1: Study calendar

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Procedures \ Study Visit	Screening/ Pre-treatment (within 30 days of start of treatment)	Day 0	Day 1 to Day of Surgery	Day of Surgery	Day 15 (±7 days)
Informed Consent	X				
Medical History	X				
Vital signs	X	X			
Physical Exam	X				
Performance Status	X				
ECG	X	X			X
Clinical Chemistries	X				
Hematology	X				
Coagulation	X				
TSH	X				
Serum Pregnancy	X*				
Urine pregnancy		X*			
Infusion of Panitumumab-IRDye800		X			
Bolus Injection of ^{111}In-Panitumumab		X			
SPECT/CT Imaging			X		
Surgical Resection				X	
Conventional Local Injection of Optical Dye				X	
Intraoperative Tumor Imaging				X	
Pathological Evaluations				X	
Adverse Events	X	X	X		X
Concurrent Medications	X	X	X		X
Follow up visit					X

*Pregnancy test will be performed on screening visit and Day 0 for women of childbearing potential.

Tissue Storage for Future Research

Research using tissues is an important way to try to understand human disease. You have been given this information because the investigators will save your excess tissue samples for future research if they are available from your standard of care. There are several things we would like you to be informed.

Your tissues and any data collected as part of this study, will be stored in the Head and Neck Tissue Repository (IRB# 030062) at Vanderbilt University Medical Center (VUMC). Samples will be labeled with a study ID code number that does not personally identify you.

The key linking the study ID code with your personal information will not be shared with researchers. Your samples may be sent outside of VUMC for research and analysis.

Identifiers will be removed from identifiable private information and/or identifiable specimens and, after such removal, the information and/or specimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you.

Saving Images for Future Research

Investigators would like to save the images and data from your SPECT/CT scans and fluorescence imaging along with surgery images for future research projects. Your data will be de identified (removing your name and medical record number), coded for confidentiality, and stored at VUMC in a secure, password protected computer. Your name and other personal identifiers will not be included in any data shared with other researchers. Your images may be sent outside of VUMC for research and analysis.

Payments for your time spent taking part in this study or expenses:

You will be paid to participate in this research study. You may receive up to a total $200 if you complete this study. You will be paid for the visits you completed according to the following schedule:
• $100 for the Infusion Day Visit
• $100 for the Imaging Visit

If you do not complete the study, for any reason, you will be paid for each study visit you do complete. We will complete a check request for you via Vanderbilt's Finance Department at the end of your participation. The check may take 4-6 weeks to process. We may ask you for your

Social Security number and address on a form before you are compensated for taking part in the study. You will also receive travel reimbursement up to $600 total with appropriate receipts and/ or documentation to study team.

If you have any questions regarding your compensation for participation and/ or travel reimbursement, please contact the study staff.

Costs to you if you take part in this study:

If you agree to take part in this research study, you and/or your insurance will not have to pay for the tests and treatments that are being done only for research. However, you are still responsible for paying for the usual care you would normally receive for the treatment of your illness. This includes treatments and tests you would need even if you were not in this study. These costs will be billed to you and/or your insurance.

You have the right to ask what it may cost you to take part in this study. If you would like assistance, financial counseling is available through the Vanderbilt Financial Assistance Program. The study staff can help you contact this program. You have the right to contact your insurance company to discuss the costs of your routine care (non-research) further before choosing to be in the study. You may choose not to be in this study if your insurance does not pay for your routine care (non-research) costs and your doctor will discuss other treatment plans with you.

Payment in case you are injured because of this research study:
If it is determined by Vanderbilt and the Investigator Dr. Eben Rosenthal that an injury occurred, then you and/or your insurance may be billed for the cost of medical care provided at Vanderbilt to treat the injury. You will be responsible for any copayments or deductibles associated with the treatment of that injury.

There are no plans for Vanderbilt or Dr. Eben Rosenthal to pay for the costs of any additional care. There are no plans for Vanderbilt or Dr. Eben Rosenthal to give you money for the injury.

Who to call for any questions or in case you are injured:
If you should have any questions about this research study or if you feel you have been hurt by being a part of this study, please feel free to contact the study doctor, **Eben Rosenthal** at (**615) 936-0708**. Your Study Coordinator will also provide you with contact information. If you cannot reach the research staff, please page the study doctor by calling (615) 322-5000 and ask the operator to page him.

For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the VUMC Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

Reasons why the study doctor may take you out of this study:
The Protocol Director may also withdraw you from the study and administration of the study agent may be stopped without your consent for one or more of the following reasons:

- Failure to follow the instructions of the Protocol Director and study staff.
- The Protocol Director decides that continuing your participation could be harmful to you.
- Pregnancy
- You need treatment not allowed in the study.
- The study is cancelled.
- Other administrative reasons.
- Unanticipated circumstances.

What will happen if you decide to stop being in this study?
If you first agree to participate and then you change your mind, you are free to withdraw your consent and discontinue your participation at any time. Your decision will not affect your ability to receive medical care for your disease and you will not lose any benefits to which you would otherwise be entitled.

If you withdraw from the study, or administration of the study agent is stopped for any reason, you will be asked to return to the clinic approximately one month from Day 0 for a safety follow up appointment (will be coordinated where possible with a routine visit).

Clinical Trials Registry:
A description of this clinical trial will be available on 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 Web site at any time.

Confidentiality:
The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed except as authorized by you or as required by law. However, there is always some risk that even de identified information might be re identified.

Patient information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

The purpose of this research study is to obtain information on the safety and effectiveness of ^{111}In panitumumab and panitumumab-IRDye800 administrations. The results will be provided to the sponsor, the Food and Drug Administration and other federal and regulatory agencies as required.

This study may have some support from the National Institutes of Health (NIH). If so, your study information is protected by a Certificate of Confidentiality. This Certificate allows us, in some cases, to refuse to give out your information even if requested using legal means.

It does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosures that you make yourself are also not protected.

Privacy:
Any samples and information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit as a result of the tests done on your samples. These tests may help us or other researchers learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Your samples may be used to make new products or tests. These may have value and may be developed and owned by the study staff, Vanderbilt University, Vanderbilt University Medical Center, and/or others. If this happens, there are no plans to provide money to you.

At any time, you may ask to have your sample destroyed. You should contact Eben Rosenthal at (615)936-0708to have your sample destroyed and no longer used for research. We will not be able to destroy research data that has already been gathered using your sample. Also, if your identity was removed from the samples, we will not be able to locate and destroy them.

There will be no costs to you for any of the tests done on your samples. You will not be paid for the use of your samples.

Study Results:

The research results will be shared with you when the study is closed out by request. The shared study results may include peer-reviewed scientific publications, news releases, and clinical trials reports at ClinicalTrials.gov.

Authorization to Use/Disclose Protected Health Information

What information is being collected, used, or shared?
To do this research, we will need to collect, use, and share your private health information. By signing this document, you agree that your health care providers (including both Vanderbilt University Medical Center and others) may release your private health information to us, and that we may use any and all of your information that the study team believes it needs to conduct the study. Your private information may include things learned from the procedures described in this consent form, as well as information from your medical record (which may include information such as HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

Who will see, use or share the information?
The people who may request, receive or use your private health information include the researchers and their staff. Additionally, we may share your information with other people at Vanderbilt, for example if needed for your clinical care or study oversight. By signing this form, you give permission to the research team to share your information with others outside of Vanderbilt University Medical Center. This may include the sponsor of the study and its agents or contractors, outside providers, study safety monitors, government agencies, other sites in the study, data managers and other agents and contractors used by the study team. We try to make sure that everyone who sees your information keeps it confidential, but we cannot guarantee that your information will not be shared with others. If your information is disclosed by your health care providers or the research team to others, federal and state confidentiality laws may no longer protect it.

Do you have to sign this Authorization?
You do not have to sign this Authorization, but if you do not, you may not join the study.

How long will your information be used or shared?
Your Authorization for the collection, use, and sharing of your information does not expire. Additionally, you agree that your information may be used for similar or related future research studies.

What if you change your mind?

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You may change your mind and cancel this Authorization at any time. If you cancel, you must contact the Principal Investigator in writing to let them know by using the contact information provided in this consent form. Your cancellation will not affect information already collected in the study, or information that has already been shared with others before you cancelled your authorization.

Eben Rosenthal, MD
Vanderbilt University Medical Center
Suite 6310, Medical Center East, South Tower
1215 21st Avenue South
Nashville, TN 37232

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this consent form and the research study has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to take part in this study.

Date	Signature of patient/volunteer

Consent obtained by:

Date	Signature
	Printed Name and Title