Institutional Review Board
Informed Consent Document for Research
Phase II

Principal Investigator: Jordan Berlin, MD **Revision Date: December 22, 2021**
Title: VICCGI1703 Phase 1/2 Study to Evaluate the Safety, Efficacy, and Novel PET/CT Imaging Biomarkers of CB-839 in Combination with Panitumumab and Irinotecan in Patients with Metastatic and refractory RAS wildtype Colorectal Cancer NCT03263429
Institution/Hospital: Vanderbilt University Medical Center

This informed consent applies to adults.

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.

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. Anyone you authorize to receive your medical record will also get this note.

1. What is the purpose of this study?

You are invited to take part in a research study (also known as a clinical trial) of the combination of a novel therapy called CB-839 in combination with standard-of-care treatment of panitumumab (VECTIBIX). You are being asked to take part in this research study because you have colorectal cancer (CRC). The purpose of this study is to test how well the drugs CB-839 and panitumumab work when used together to keep your cancer from growing and spreading.

Glutamine is a molecule that plays a variety of roles that are required for cell survival. Compared to normal cells, some cancer cells have increased glutamine metabolism that drives their growth and progression. The study drug CB-839 works by blocking a key regulator of glutamine metabolism.

Some cancer cells have too much epidermal growth factor receptor (EGFR) which is a protein on the surface of cells that normally helps your cells grow and divide. Having too much EGFR can cause cancer cells to grow faster. The study drug panitumumab works by blocking the epidermal growth factor receptor (EGFR) to stop the growth and spread of cancer cells. Panitumumab is currently FDA-approved for the treatment of certain types of CRC.

CB-839 and panitumumab have not yet been FDA-approved to use together for the treatment of your disease.

To allow you to make an informed decision as to whether or not you want to take part in this research study, this document describes the purpose of the study, your rights and obligations, the procedures needed by the study, and the possible benefits and risks of participating in the study. Please take time to read the following information carefully. Feel free to talk with your doctor, nurse, family, or friends before deciding. If you have any questions, you may ask the study doctor, Dr. Berlin, for more information.

As a part of the study we are asking you to undergo a pre-treatment tumor biopsy and two positron emission tomography (PET)-CT scans in order to measure the amount of glutamine metabolism in your cancer. We are also asking you to provide blood to look at circulating markers to explore how they affect health and disease.

The study is being sponsored by Vanderbilt. CB-839 is being provided by the company Calithera. Panitumumab will be obtained as standard of care from commercial supply. The doctor in charge of this study is Jordan Berlin, MD.

Approximately 29 participants from Vanderbilt will take part in this study.

2. What will happen and how long will you be in the study?

If you give your consent to be in this study by signing this form, you will have tests and procedures (called "**screening**") done. These are done to reduce the risks of taking part in this study and to make sure it is okay for you to be in the study.

Biospecimens will be collected in this study. Biospecimens may include any of the following: blood, tissue, saliva, urine, bone marrow, cells, etc. Most biospecimens contain DNA, which is the genetic code for each person.

It is possible that after these tests are reviewed, you will not be able to be in the study. There may be other reasons why you cannot be in this study. These reasons will be discussed with you by your study doctor or the clinic staff.

Your samples and information about you may be made available to others to use for research in the future. 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 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, and/or others. If this happens, there are no plans to provide money to you.

Screening

You will need to have the following exams, tests or procedures to find out if you can be in the study. The information and samples collected as part of these screening activities will be kept and used like the rest of the study results. These tests are sometimes part of regular medical care. They may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated.

Before entering the study (screening and pre-treatment assessments), the following will be done:

- **Informed Consent**: Discussion of this study and review and signing of this Informed Consent Form
- **Demographics**: Recording of your demographic information, including your age, sex, and race/ethnicity
- **Medical history:** You will be asked about your health and any illnesses, surgeries, and treatments you may have or had in the past. You will be asked about medicines you are taking (including over-the-counter medicine, vitamins or herbal treatments).
- **Physical examination:** You will receive a complete physical examination including measurement of height and weight. This will also include a skin exam. Your performance status (your ability to carry out your daily activities) will be assessed.
- **Vital signs:** Your temperature, breathing, blood pressure, and heart rate will all be checked.
- **Concomitant medications:** You will be asked what medicines you are taking.
- **Pregnancy Test:** If you are a woman and can have children, you will have a blood or urine test to be sure you aren't pregnant prior to starting study therapy.
- **Urine test:** You will be asked to provide a urine sample to check your health.

- **Blood tests (about 4-5 tablespoons):**
  - **Blood tests to check your health and ability for your blood to clot:** A small amount of your blood will be drawn from a vein for lab tests, including white blood cell count with differential, hemoglobin, hematocrit, platelet count, sodium, potassium, chloride, bicarbonate or carbon dioxide, blood urea nitrogen, creatinine, glucose, total bilirubin, AST, ALT, alkaline phosphatase, calcium, albumin, total protein, magnesium, PT/INR, and PTT
  - **Blood test for pregnancy:** If a urine pregnancy test result cannot be confirmed as negative, a blood pregnancy test will be performed (Only for women able to have children). Also, a blood test for pregnancy will be performed prior to (within 24 hours) each research PET scan if you are able to have children.
- **CT or MRI Scans:** We will require these scans to tell us where your tumor(s) are located and what size they are.
- **Pre-treatment biopsy**: Prior to starting treatment on the main study, a biopsy of your primary tumor tissue or any tissue to which the tumor has spread will be collected. This procedure will take one visit to the clinic. Your research doctor will tell you what area(s) of your body can be biopsied. Your research doctor, with your input and consent, will select only one area to biopsy. This is the case even if your cancer has spread to multiple areas. Before the biopsy, you will discuss the procedure with the doctor who will perform the biopsy. You will be asked to sign a separate consent form with the doctor that performs the procedure. You will sign only after an explanation of the potential risks.

  If you have a core needle biopsy: If you have a core needle biopsy done, a medium sized, hollow needle will be inserted into your tumor to withdraw small cylinders (or cores) of tumor tissue. You will receive local anesthesia (you will be awake, but the biopsy site and immediately surrounding area will be numbed). The needle will be inserted 3 to 6 times to obtain the samples.

  If you have a surgical biopsy: There are two types of surgical biopsies (incisional and excisional). If you have an incisional biopsy, a small area of tissue, containing tumor tissue and some surrounding tissue, will be cut from the biopsy site. If you have an excisional biopsy done, the entire tumor area is removed.

  You will be given local anesthesia to numb the area. You may also be given medicine to relax you in addition to the numbing agent. A small cut will be made to access the area to access your tumor, and tissue will be cut out and sent to a pathology lab for review.

  Your samples will be used for research purposes, including disease-related mutational testing and the development of a tumor model, which will help researchers learn more about colorectal cancer.

  Your 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 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, and/or others. If this happens, there are no plans to provide money to you.

- **Research PET/CT Imaging:** These images will allow us to detect your tumor and develop the best methods to image the tumor. This investigational imaging will also allow us to identify changes that happen in the biology of your tumor after taking the study drugs. Research PET/CT images will be collected at the following visit:
  - Prior (-7 days) to Day 1 of Cycle 1

  You will be injected with one investigational radiotracer (radioactive compounds that can be detected on a PET scan) called ^{18}F-FSPG. Prior to this injection, you will be asked about the last time you ate and your blood sugar level may be tested.

  After administration of ^{18}F-FSPG, you will be asked to lie on your back on the PET scanning table with your arms resting above your head. A series of images will be collected for each PET session. A CT scan (90 seconds) will also be collected following collection of all images for each PET session. You will be asked to use the restroom immediately, even if you don't feel the urge, in order to empty your bladder. The total time you will be scanned will be approximately 2.5 hours, and the total time you will need to be in the PET facility will be approximately 3 hours.

  During each radiotracer injection, blood (totaling approximately 3 teaspoons) will be collected for research to assess how the radiotracer circulates through your blood stream.

  Also, you must refrain from smoking after midnight the night before or the day of each research scan.

  You will be contacted via telephone within 24 – 48 hours of receiving the scan. You will be asked questions about any side-effects you may have experienced within 24 hours of the scan.

Before participating you should consider if these procedures will affect any insurance you currently have, or may purchase in the future, and seek advice if necessary from your insurance company.

Treatment Phase, End of Treatment (EOT) Visit, and Follow up

If you qualify to participate in the study, the following exams/tests/procedures will be done:

- **Vital Signs and Weight**: heart rate, blood pressure, respiratory rate, weight, height (collected only in cycle 1), and temperature will be recorded as follows:
  - Day 1 and Day 15 of each cycle
  - End of Treatment (EOT) visit
  - Follow-up visit
- **Physical Exam (including skin exam):**
  - Day 1 and Day 15 of each cycle
  - EOT visit
  - Follow-up visit
- **Assessment of performance status:**
  - Day 1 and Day 15 of each cycle
  - EOT visit
  - Follow-up visit
- **Side-effects:** At each study visit during treatment and after treatment, you will be asked about any side-effects you may be having.

- **Concomitant medications:** At each study visit during treatment and at the EOT visit you will be asked what medicines you are taking.
- **Blood tests to check your health:** A small amount of your blood (about 2-3 tablespoons) will be drawn from a vein for lab tests at the following visits:
  - Day 1 and Day 15 of all cycles
  - EOT visit
  - Follow-up visit
  - You may have blood drawn to check your health at other times if your doctor thinks it is necessary.
- **Blood tests for biomarkers:** This blood will allow us to identify changes that happen in the biomarkers after you have taken the study drugs. An additional blood amount (no more than 2 teaspoons) will be drawn from your veins for the analysis of DNA, RNA and protein biomarkers in the blood at the following visits:
  - Day 1 and Day 28 of Cycle 1
  - EOT visit
- **Research PET/CT Imaging:** These images will allow us to detect your tumor and develop the best methods to image the tumor. This investigational imaging will also allow us to identify changes that happen in the biology of your tumor after taking the study drugs. Research PET/CT images will be collected at the following visits:
  - Any time during week 4 for Cycle 1 (Days 22 – 28 of Cycle 1) or pre-treatment on Cycle 2 Day 1

  You will be injected with one investigational radiotracer called ^{18}F-FSPG. Prior to this injection, you will be asked about the last time you ate and your blood glucose level may be tested.

  After administration of ^{18}F-FSPG, you will be asked to lie on your back on the PET scanning table with your arms resting above your head. A series of images will be collected for each PET session. A CT scan (90 seconds) will also be collected following collection of all images for each PET session. You will be asked to use the restroom immediately after, even if you don't feel the urge, in order to empty your bladder. The total time you will be scanned will be approximately 2.5 hours, and the total time you will need to be in the PET facility will be approximately 3 hours.

  During each radiotracer injection, blood (no more than 3 teaspoons) will be collected for research to assess how the radiotracer circulates through your blood stream.

  Also, you must refrain from smoking after midnight the night before or the day of each research scan.

  You will be contacted via telephone within 24 – 48 hours of receiving the scan. You will be asked questions about any side-effects you may have experienced within 24 hours of the scan.
- **CT or MRI Scans:** Scans are used to measure the size of your tumors. A scan of the brain may be done if the doctor decides it is needed. Scans and, if applicable, photographs, will be done at the following visits:
  - Every 8 weeks after starting study treatment on Cycle 1 Day 1
  - Follow-up visit
  - If you come off study for reasons other than progression of your disease, you will continue to have scans every 8 weeks.
  - You may have additional scans if your doctor thinks it is clinically necessary.
- **Treatment plan:**
  - You will take CB-839 in a pill form, by mouth, twice every day

- You will receive a 60 or 90 minute IV infusion of panitumumab on Day 1 and Day 15 of each 28 day cycle

Instructions Regarding CB-839

- Dosing Instructions
  - CB-839 should be taken twice daily with food at approximately the same time each morning and evening
    - Approximately 12 hours apart
  - Missed doses of CB-839 can be made up during the same day if you remember. However, if the last dose was taken less than 6 hours in the past or if the next dose is used in less than 6 hours, then the missed dose should be skipped.
  - If you vomit, do not re-take your dose of CB-839
  - Depending on the other medications you are taking, you may be asked to take CB-839 with an acidic beverage such as orange juice.
- Dosing Diary
  - You will be given a diary to complete while you are taking the study drugs. This is to record the date, time, and how much study drug you have taken. You will be asked to return your completed diary when you come to the clinic for each visit.
  - You will be asked to confirm if you took your dose with food.
  - If you are asked to take your doses with acidic beverages, you will be asked to record information about this on the dosing diary.
  - You may also record any problems you have had while taking the study drug or any questions you may have for the study doctor or nurse. You will be asked to bring any unused study drug along with any empty bottles with you to each clinic visit.

How long will I be in the study?

You will keep taking the study drugs until:

- Your disease gets worse, or
- You get bad side effects from the treatment that you cannot tolerate, or
- You wish to stop the study, or
- You are not able to follow the requirements of the study, or
- The study is canceled

Because of these reasons, we cannot predict the length of time that you will be on study. You will be closely followed by the research nurse while on study and will be asked to come back to the cancer clinic for a follow up visit within 28 days (+/- 7 days) from your last dose of study drugs. You will also be followed every 3 months after your last dose of study drug until the study comes to an end, you withdraw consent, or 1 year after your final study drug treatment, whichever comes first.

If you have a serious side effect during the study, the study doctor will ask you to visit the office for follow-up examinations, even after you have completed your regular study visits.

3. 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.

4. Side effects and risks that you can expect if you take part in this study:

You may have side effects while on this study. Ask the study doctor if you have any questions about the side effects described here.

Everyone in the study will be watched carefully for any side effects. Side effects may be mild, moderate, or serious. If you experience a side effect, the study staff may give you medicines to help lessen these effects. Some side effects may go away as soon as you stop taking the drug. In some cases, side effects can be serious, long-lasting, may never go away, or may lead to death. Rare cases of sudden death have occurred in patients with advanced cancer.

What side effects could CB-839 cause?
Listed below are side effects reported from 83 patients that took telaglenastat (CB-839) by itself at doses between 600mg-800mg taken twice daily as a treatment for solid cancers as of January 23, 2020:

<u>Very common side effects</u> in people taking CB-839 include the following (10% or more of cancer patients):
- Nausea
- Decrease in appetite
- Constipation
- Abnormal liver function tests (an increase in specific laboratory tests, such as: alanine aminotransferase, aspartate aminotransferase, gamma-glutamyl transferase, and alkaline phosphatase) which may indicate liver damage. Changes to date have been reversible and have not generally recurred on dose reduction
- Photophobia- sensitivity to light

What side effects could panitumumab cause?

<u>Very common: (may occur in 10% or more of cancer patients):</u>

- Feeling tired, lack of energy
- Abdominal pain
- Nausea
- Diarrhea
- Vomiting
- Constipation
- Decreased levels of magnesium in the blood (may cause symptoms such as muscle spasms, cramps, seizures and others)
- Swelling of the face, arms, hands, lower legs, ankles, and feet
- Cough
- Reddening of the skin

- Acne
- Itching of the skin
- Infection of the skin around fingernails or toenails
- Breaking, cracking, or peeling of the skin
- Rash
- Dry skin
- Difficulty breathing
- Cough
- Fever

<u>Less common side effects</u> seen in people taking panitumumab include the following (between 1% and 10% of cancer patients):

- Inflammation of the mouth and lips
- Inflammation of the mucous membrane (tissue that line body cavities or canals such as the throat, nose, mouth, urethra, rectum, and vagina)
- Eye/eyelid infection
- Eye/eyelid irritation
- Teary, itch, dry, red eyes or blurry vision
- Redness of the eye
- Growth of eyelashes
- Breaking, cracking, or peeling of the skin
- Nail disorders such as breaking or splitting fingernails or toenails
- Infusion-related reactions (such as fever, chills, shaking, decrease in blood pressure, slowed heart rate, sudden sever shortness of breath, life-threatening loss of heart or lung function, joint or muscle pain, and rash)
- Dehydration (loss of body water)
- Decreased levels of potassium in the blood (may cause symptoms such as muscle cramps, weakness, nausea, diarrhea, and others)
- Pulmonary embolism (blood clot in the lung)
- Dry mouth
- Chills
- Bleeding from the nose

<u>Uncommon side effects seen in people taking panitumumab include the following (Between 0.1% and 1% of cancer patients):</u>

- Scarring of the lungs that leads to difficulty breathing

<u>Serious side effects in people taking panitumumab</u>: No event occurred in more than 14 % of everyone treated. Please note that some of these events have been previously stated above, so some have occurred more frequently but with less severity. Serious adverse events seen in people taking panitumumab include:

- Feeling tired, lack of energy
- Abdominal pain
- Nausea
- Diarrhea
- Vomiting

- Inflammation of the mucous membrane (tissue that line body cavities or canals such as the throat, nose, mouth, urethra, rectum, and vagina)
- Decreased levels of magnesium in the blood (may cause symptoms such as muscle spasms, cramps, seizures and others)
- Dehydration (loss of body water)
- Decreased levels of potassium in the blood
- Swelling of the hands and feet
- Cough
- Reddening of the skin
- Skin acne
- Itching of the skin
- Infection of the skin around fingernails or toenails
- Breaking, cracking, or peeling of the skin
- Rash
- Inflammation of the skin
- Infusion-related reactions (such as fever, chills, shaking, decrease in blood pressure, slowed heart rate, sudden sever shortness of breath, life-threatening loss of heart or lung function, joint or muscle pain, and rash)
- Pulmonary embolism (blood clots in the lung)
- Sepsis (infection in the blood)
- Septic death (infection in the blood resulting in death)
- Abscesses (wound filled with pus) requiring incisions and drainage
- Dehydration (loss of body water)

The side effects listed above are based on all side effects reported in subjects and includes those effects considered to be related to the study drugs. Everyone in the study will be watched carefully for any side effects. If you experience a side effect, the study staff may give you medicines to help lessen these effects. Side effects may be mild, moderate, or serious. Some side effects may go away as soon as you stop taking the study drugs.

You may experience side effects from some of the procedures in this study:

Blood samples: When giving blood or when having a cannula inserted in your arm, you may feel faint, or experience mild pain, bruising, irritation or redness at the site. In rare cases, you may get an infection or damage to nerves at the site. A cannula is a small tube that stays in your arm so that you will not need a lot of needle sticks when blood is drawn. Study staff will remove the cannula before you leave the clinic.

Computerized Tomography (CT scan): A CT scan is a specialized X-ray test that takes images of the body. The amount of radiation used to do a CT scan is greater than with a normal X-ray. You may feel some discomfort or anxiety when lying inside the scanner.

- If contrast material (iodine) is used during the CT scan there is slight risk of developing an allergic reaction. The reaction can be mild (itching, rash) or severe (difficulty breathing or sudden shock). Death resulting from an allergic reaction is rare. Most reactions can be controlled using medication. Be sure to tell your doctor if you have allergies of any kind (such as hay fever, iodine allergy, eczema, hives, or food allergies) or have had a previous reaction to medications or contrast material.
- The contrast material used during CT scanning can cause water loss or damage to the kidneys that may lead to kidney failure. This is a concern if you have poor kidney function, dehydration, or diabetes, especially if you take Glucophage® (metformin) to control your diabetes.

Magnetic Resonance Imaging (MRI): MRI scans use strong magnetic fields and radio waves to produce an image of the inside of the body. There are no known harmful effects from the strong magnetic field used in MRI scans. However, the magnet is so powerful that it can affect any unsecured metal objects, which can be pulled towards the magnet. The magnet may affect pacemakers, artificial limbs, and other medical devices or implants that contain metal. You should discuss any devices in your body with the study staff. You may feel some discomfort or anxiety when lying inside of the scanner.

- If contrast material is used during the MRI scan there is slight risk of developing an allergic reaction. However, most reactions are mild and can be controlled using medication.
- For patients that need an MRI scan and have reduced kidney function there is a chance of developing "Nephrogenic Systemic Fibrosis", a condition that can cause thickening and itchiness of the skin, stiffening of the joints and possible reduction in the ability to move around. This condition is related to the MRI contrast agent gadolinium and occurs mostly in patients with severe kidney disease. The risk to patients with mild kidney impairment is thought to be small.

Radiation Risks:
This research study may involve exposure to radiation from up to 2 CT scans of the Chest, Abdomen and Pelvis, 1 CT-Guided Biopsy procedure, and 2 PET/CT scans. This radiation exposure is not necessary for your medical care and is for research purposes only. The total amount of radiation that you may receive by participating in this study is about 19% more than the amount allowed in a year for people who are exposed to radiation as part of their work. Please tell your doctor if you have taken part in other research studies or received any other medical care recently involving radiation. If you are pregnant or breast feeding, you SHOULD NOT participate in this research study. To protect your bladder from the effects of the injected radioactive substances, you should drink plenty of fluids and empty your bladder every two hours for at least the first six hours after you have each PET/CT scan.

Risks of Investigational Imaging Tracer: Although there are no known side effects to the investigational PET tracers when given in an IV, there is a rare chance of an allergic reaction or other side effect to radioactively labeled drugs. This can range from a mild skin rash to a more severe reaction, such as throat tightness, difficulty breathing, lowered blood pressure and rarely, death.

Pregnancy and Birth Control: Because the drugs and investigational imaging tracer being tested in this study may affect an unborn baby, women should not take part in this study if:

- You are pregnant or planning to become pregnant.
- You are currently breastfeeding.

You should not become pregnant while you are in this study because the drugs and investigational imaging tracer in this study may affect an unborn baby.

Women who can get pregnant will need to use two forms of birth control while in this study and for 4 months after your last dose of study drug. Check with the study doctor about what kind of birth control methods to use.

To prevent pregnancy in a female partner or to prevent exposure of any partner to the study treatment from a male subject's semen, male subjects will need to use birth control while in this study, as will their partner. Birth control must be used in male subjects from the beginning of the study until 4 months after the last dose of study drug.

If you get pregnant during this study, call the study doctor right away. You may be asked questions later about the pregnancy and the baby.

Privacy Risk: One risk of giving samples for this research may be the release of your name that could link you to the stored samples and/or the results of the tests run on your samples. This may cause problems with insurance or getting a job.

Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums. Employers with 15 or more employees may not use your genetic information that comes from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

To prevent this, these samples will be given a code. Only the study staff will know the code. The name that belongs to the code will be kept in a locked file or in a computer with a password. Only (investigator's name and/or other's names) will have access to your name.

5. Risks that are not known:

Because this treatment combination is investigational, meaning non-FDA approved, there may be risks that we do not know about at this time.

6. Payment in case you are injured because of this research study:

If it is determined by Vanderbilt and the Investigator that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided **at Vanderbilt** to treat the injury.
There are no plans for Vanderbilt to pay for any injury caused by the usual care you would normally receive for treating your illness or the costs of any additional care. There are no plans for Vanderbilt to give you money for the injury.

7. Good effects that might result from this study:

a) The benefits to science and humankind that <u>might</u> result from this study. Knowledge from this study may help doctors better understand colorectal cancer, treatment for your condition, or help determine who is more likely to benefit or who is more likely to have side effects from the study drugs. It may also help future patients.

b) The benefits you might get from being in this study. Taking part in this study may or may not make your health/condition better, and may or may not have direct benefit to you.

8. Other treatments you could get if you decide not to be in this study:

You may choose not to take part in this study.

You may choose to continue to get regular care from your own doctor. This may include other treatments available in your country.

Alternately you might decide to:
- Take part in another study

- Get no treatment at this time.

Talk with the study doctor, or your family doctor, about your treatment choices.

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

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

10. Reasons why the study doctor may take you out of this study:

You may be asked to leave the study if:

- The results of certain tests show that you are not right for this study or for the study drug.
- You do not follow study instructions for treatment or follow-up visits.
- You get new health problems during the study that might not work well with the study set-up.
- You get pregnant or decide that you want to become pregnant.
- The study doctor thinks it is best for you to stop.

New information may become available or known that might affect your choice to stay in the study. Such information will be shared and discussed with you. This new information might include:

- Safety issues with the study drug

Dr. Berlin or the regulatory authorities may choose to stop the study at any time. We will give you the reason at that time.

11. What will happen if you decide to stop being in this study?

Your participation in the study is voluntary. You may choose to stop taking part in the study at any time, without giving a reason. If you decide to stop being part of the study, you should tell your study doctor. Your decision will not affect your medical care now or in the future. It will not affect other benefits you receive outside of the study.
If you decide to leave the study, you and the study doctor will discuss the best way to do this. We will ask you to return any leftover study drug. We will ask you for the names and contact information of some of your family members, friends and other doctors. We may contact these people if we are not able to contact you during the study.

All the data and samples collected before you left the study will still be used for the study.

12. 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 Vanderbilt Ingram Cancer Center at (877) 936-8422 or (615) 322-5000 and ask for Dr. Jordan Berlin.

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 Vanderbilt University Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

13. Clinical Trials Registry:

A description of this clinical trial will be available on www.clinicaltrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

14. Confidentiality:

Vanderbilt may share your information, without identifiers, to others or use it for other research projects not listed in this form. Vanderbilt, Dr. Berlin, and his staff will comply with any and all laws regarding the privacy of such information.

There are no plans to pay you for the use or transfer of this de-identified information.

15. Authorization to Use/Disclose Protected Health Information

All efforts, within reason, will be made to keep your protected health information (PHI) private. PHI is your health information that is, or has been gathered or kept by Vanderbilt as a result of your healthcare. This includes data gathered for research studies that can be traced back to you. Using or sharing ("disclosure") such data must follow federal privacy rules. By signing the consent for this study, you are agreeing ("authorization") to the uses and likely sharing of your PHI. If you decide to be in this research study, you are also agreeing to let the study team use and share your PHI as described below.

As part of the study, Dr. Berlin and his study team may share the results of your study and/or non-study linked exams, lab tests, PET/CT scans, CT or MRI scans, as well as parts of your medical record, to the groups named below. These groups may include people from Vanderbilt University Medical Center and its authorized representatives, Calithera Biosciences, the Federal Government Office for Human Research Protections, the Vanderbilt University Institutional Review Board, Vanderbilt Scientific Review Committee, National Cancer Institute, Food and Drug Administration, and insurance companies for billing purposes. Federal privacy rules may not apply to these groups; they have their own rules and codes to assure that all efforts, within reason, will be made to keep your PHI private.

The study results will be kept in your research record for at least six years after the study is finished. At that time, the research data that has not been put in your medical record will be kept for an unknown length of time. Any research data that has been put into your medical record will be kept for an unknown length of time.

Unless told otherwise, your consent to use or share your PHI does not expire. If you change your mind, we ask that you contact Dr. Berlin in writing and let him know that you withdraw your consent. His mailing address is 2220 Pierce Ave 777 PRB, Nashville, TN 37232-6307. At that time, we will stop getting any more data about you. But, the health data we stored before you withdrew your consent may still be used for reporting and research quality.

You have the right to see and copy the PHI we gather on you for as long as the study doctor or research site holds this data. To ensure the scientific quality of the research study, you will not be able to review some of your research data until after the research study is finished.

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