PRINCIPAL INVESTIGATOR: Tim Greten, M.D.

STUDY TITLE: Phase II trial of VB-111 in Combination with Nivolumab in Patients with Metastatic Colorectal Cancer (mCRC)

STUDY SITE: NIH Clinical Center

Cohort: Affected Patient

Consent Version: 01/22/2021

WHO DO YOU CONTACT ABOUT THIS STUDY?

Tim Greten, MD, by phone at 240-760-6114 or email Tim.greten@nih.gov

KEY INFORMATION ABOUT THIS RESEARCH

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). This section provides the information we believe is most helpful and important to you in making your decision about participating in this study. Additional information that may help you make a decision can be found in other sections of the document. Taking part in research at the NIH is your choice.

You are being asked to take part in this study because you have microsatellite stable (MSS) colorectal cancer that has spread to the liver. Colorectal cancer tumors are often characterized by an "MSI status," meaning they will either be **M**icro**s**atellite **I**nstable (MSI) or **M**icro**s**atellite **S**table (MSS). MSI tumors can't correct mistakes that occur when DNA is copied in the cell and as a result have a lot of microsatellites - short, repeated pieces of DNA. MSS tumors do not have large number of microsatellites, but they still have a lot of mistakes in DNA and abnormal number of chromosomes.

The purpose of this study is to see if using a combination of VB-111 and nivolumab is safe and will cause your tumors to shrink.

The use of VB-111 in this study is considered investigational which means it has not been approved by the U.S. Food and Drug Administration (FDA) to treat colorectal cancer. However, the FDA has given us permission to use VB-111 in this study. VB-111 is a genetically inactivated adenovirus, modified in the lab to disrupt blood vessels which feed the tumors. It also and produces human proteins that help to activate your immune system. Adenoviruses are very common viruses that cause cold-like symptoms, sore throat, bronchitis, pneumonia, diarrhea, or pink eye. You can get an adenovirus infection at any age and most likely you have

already had one. You will not be infected by VB-111 that we give you, but you may have symptoms similar to a cold.

Nivolumab has been approved by the U.S. Food and Drug Administration (FDA) for patients with microsatellite unstable (MSI), but not microsatellite stable (MSS) colorectal cancer. Nivolumab is an agent that targets and blocks a pathway that prevents your immune system from effectively fighting your cancer.

There are other standard of care drugs and/or procedures that may be used to treat your disease, and these can be given to you by your regular cancer doctor if you are not in this study. For example: there is chemotherapy and group of drugs called kinase (regorafenib) or phosphorylase (tipiracil) inhibitors. You can also participate in another clinical trial using drugs called immune checkpoint inhibitors (such as durvalumab, cabozantinib or pembrolizumab). The treatment given in this study and the known possible side effects may or may not be significantly different than if you were to receive standard care or being in another clinical trial. For example: chemotherapy cause fatigue, hair loss, bruising and bleeding, infection, low blood cell counts. Inhibitors are known to cause changes in blood counts, high blood pressure and slow wound healing. Immune checkpoint inhibitors may cause inflammation of the lung, intestines or liver, and kidney, heart, or problems of the nervous system. Any of these treatments can cause nausea, vomiting, diarrhea and rash.

One study drug, nivolumab, is a checkpoint inhibitor and has similar side effects to those listed above. The most common side effects of VB-111 include flu-like symptoms, such as fever, chills, tiredness, headache and muscle pain.

If you decide to join this study, here are some of the most important things that you should know that will happen:

- First, we will perform tests to find out if you fit the study requirements. We will do standard blood tests and scans to test your health and see the status of your disease.
- It is very important to us to understand how your tumor is affected by study treatment. To answer this question, we will collect tumor biopsies (samples) from you before treatment and after starting treatment. You can only take part in this study if you agree to these biopsies. The most common risks of biopsy include pain and the chance of bleeding at the site of the biopsy. The site of biopsies will be determined by a group of doctors to obtain the safest possible location, most commonly the liver.
- If you fit the study requirements and decide to take part, you will start your treatment with VB-111 and nivolumab and then we will need to see you at the Clinical Center every 14 days while you are receiving treatment. You will get your treatment without hospitalization, except that you might be admitted for biopsy and spend a night in the hospital. Each visit should last no more than 8 hours.
- If your doctor is convinced that you have unacceptable side effects caused by one of treatment drugs, this drug will be stopped, and you may continue treatment with the other drug if your study doctor finds that it is in your best interest.

- As described above and later in more detail in this consent form, you may have side effects if you take part in this study. Some can be mild or very serious and may include death. You will be seen regularly during the study. You will have clinical, laboratory, and imaging tests to see how you are doing and see how your disease is responding. We will also collect required samples from you (such as: blood and urine) for clinical purposes.
- After the study treatment has ended, we would like to see you in the Clinical Center monthly for 3 months to check on your health. After that we are planning to contact you by phone or e-mail to learn about your health status, and to see how you are doing, for the rest of your life or until the study is stopped. If you stop treatment for reasons other than worsening of your disease, we will continue to invite you for imaging studies approximately every 8 weeks until worsening of your disease. You can have these studies at home institution and send us results.

You should not donate blood while participating on this study, and for at least 5 month (if you are women) and 7 months (if you are men) following your last infusion of nivolumab or 2 month following last infusion of VB-111 whichever is the longer time period.

This study may benefit you by shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the cancer. Even if you do not benefit from this study, the results from our research will help others in the future.

You are free to stop taking part in the trial at any time. If you decide to stop, the study doctor may ask you to agree to certain tests to make sure it is safe for you to stop.

The remaining document will now describe more about the research study. This information should be considered before you make your choice. Members of the study team will talk with you about the information described in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers.

If the individual being asked to participate in this research study is not able to give consent to be in this study, you are being asked to give permission for this person as their decision-maker. The term “you” refers to you as the decision-maker and/or the individual being asked to participate in this research, throughout the remainder of this document.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

This is a research study. The purpose of this study is to see if treating of your cancer with combination of VB-111 and nivolumab is safe and will cause your tumors to shrink.

We are asking you to join this research study because you have microsatellite stable (MSS) colorectal cancer that has spread to the liver. Colorectal cancer tumors are often characterized by an "MSI status," meaning they will either be **M**icro**s**atellite **I**nstable (MSI) or **M**icro**s**atellite **S**table (MSS). MSI tumors can't correct mistakes that occur when DNA is copied in the cell and as a result have a lot of microsatellites - short, repeated pieces of DNA. MSS tumors do not have large number of microsatellites, but they still have a lot of mistakes in DNA and abnormal number of chromosomes.

VB-111 is considered investigational which means it has not been approved by the U.S. Food and Drug Administration (FDA) to treat colorectal cancer. VB-111 is designed to destroy blood vessels which feed the tumors and produce human proteins, that help to activate your immune system.

Nivolumab has been approved by the U.S. Food and Drug Administration (FDA) for patients with microsatellite unstable (MSI), but not microsatellite stable (MSS) colorectal cancer. Nivolumab is an agent that targets and blocks a pathway that prevents your immune system from effectively fighting your cancer.

WHAT WILL HAPPEN DURING THE STUDY?

VB-111 and/or nivolumab will be given to you by IV (through an intravenous catheter, a small plastic tube that is put into a vein, usually in your arm) on Day 1 of treatment cycles (1 Cycle = 14 days).

VB-111 will be started on cycle 1 and continue every +3 cycles (cycles 4, 7, 10 and so on).

Nivolumab will be started on cycle 2 and continue every cycle.

If your doctor is convinced that you have unacceptable side effects caused by one of treatment drugs, this drug will be stopped, and you may continue treatment with the other drug if your study doctor finds that it is in your interest. Treatment will continue until you have unacceptable side effects (both drugs) or you are no longer benefiting from the study therapy.

Treatment and all study related procedures will be done during outpatient visits without planned hospitalization. However, we might still choose to keep your overnight if needed for biopsies and other situations that arise.

Before you begin the study

Before you begin this study, you will need to have standard clinical exams and tests to make sure you are eligible for this study. The exams and tests are part of regular cancer care. Most of these tests will be done under a separate protocol.

You will be asked to provide a pathology report or similar documentation to confirm your diagnosis. If this documentation is not available, we will perform a biopsy (collect a sample of your tumor) to confirm your diagnosis.

You also need to agree to participate in our sample collection protocol 11C0112.

If treatment does not start within 28 days after enrollment to this study, some tests may need to be repeated.

During the study

Procedures before treatment performed only once:

- Blood test to evaluate human leukocyte antigen (HLA). HLAs are markers on most cells in your body and your immune system uses these markers to recognize which cells belong in your body and which do not.
- Echocardiogram - ultrasound of your heart to evaluate your heart if your study doctor thinks it is needed

Ongoing procedures before treatment and with every cycle:

- Physical examination, including weight and vital signs.
- Review of your symptoms, medications and your ability to perform your normal activities.
- Discussion of any symptoms you might be having
- Routine blood tests to find out if you are anemic, have low blood counts, and if your liver, kidneys, thyroid, clotting system and other organs are working well.
- Blood tests to check tumor markers.
- Electrocardiogram (EKG – a record of your heartbeat) to evaluate your heart.
- Pregnancy test if you are a woman who can have children.

Ongoing procedures before treatment and every 4 cycles:

- Imaging assessments/scans – a CT (a series of x-ray images taken of parts of your body) of chest, abdomen and pelvis.

Blood draws

You will have blood drawn to monitor your health during the study (about 4 tablespoons each visit/cycle).

Additional research testing

In addition to performing the tests described above, we will also do tests for research purposes only. Two required tumor biopsies will be collected before therapy and after 2 or 6 weeks on study. If your disease gets worse before you can have this second biopsy, your doctor might choose to collect the biopsy at the time your disease worsens. Please see section Risks from Biopsy for possible risks of biopsy. If you have a biopsy during screening to confirm your diagnosis, the baseline biopsy should not need to be repeated. You can take part in the study only if you agree to have the biopsy procedures.

Tumor samples collected for research purposes on this study will be used to find out if VB-111 can be detected in the tumor.

When you are finished taking the drugs (treatment)

Approximately 28, 60 and 90 days after you have finished taking the study drug, you will be asked to return to Clinical Center for a safety follow up visits. At these visits, you will be asked questions about your health, get a physical exam and undergo blood tests.

If you have been taken off treatment for reasons other than worsening of your disease, you will continue to have imaging studies approximately every 8 weeks until worsening of your disease. You can have these studies at home institution and send us results.

If you are unable to return for these visits, we will obtain the information from you by telephone or e-mail.

Once you stop coming to Clinical Center for safety visits and your scans, we will call or e-mail you every 6 months to ask you about your general well-being.

HOW LONG WILL THE STUDY TAKE?

You will come for study treatments every 14 days until your disease gets worse or you have unacceptable side effects at which time we will stop treatment.

Visits will range from 4-8 hours in length.

After stopping treatment, we would like to see you in the NIH Clinical Center monthly for three months and follow you after that for the rest of your life.

If you stop treatment for reasons other than worsening of your disease, we would like to invite you for imaging studies approximately every 8 weeks until worsening of your disease.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

We plan to have up to 27 people take part in this study.

WHAT ARE THE RISKS AND DISCOMFORTS OF BEING IN THE STUDY?

The drug used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last longer.
- Some side effects may be serious and may even result in death.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drugs to try to reduce side effects.

Risks of VB-111

The most frequent side effects related to VB-111 have been flu-like symptoms, including fever, chills and fatigue. These events usually occur on the day of study treatment (often starting about 6 hours after the infusion) and resolve on the same day. To control these symptoms, an anti-fever drug will be given to you prior to VB-111 infusion.

The table below presents the common side effects that were seen in patients treated with VB-111 according to their observed frequencies:

MOST COMMON, SOME MAY BE SERIOUS In 100 people receiving VB-111, more than 20 may have:
• Fever
• Chills
• Tiredness
• Nausea
• Headache

VERY COMMON In 100 people receiving VB-111, 10 to 20 may have:
• Vomiting
• Mild diarrhea
• Constipation
• High blood pressure
• Shortness of breath
• Muscle weakness
• Worsening of your disease

COMMON In 100 people receiving VB-111, 5 to 10 may have:
• Flu like illness • Cough • Dizziness • Temporary elevation of enzymes in the liver – which may be an indicator of liver damage • Prolonged PTT (test of blood clotting) which may increase the risk of bleeding • Decreased platelet count, which may increase the risk of bleeding/bruising • Decrease of mineral levels in the blood (Sodium and Potassium) • Elevation of blood glucose levels • Decrease in red blood cells • Elevation of protein level in the urine • Low blood pressure • Pain, including: abdominal pain, back pain, muscle pain and joint pain • Loss of strength • Loss of appetite • Difficulties sleeping • Urinary tract infection • Heart rate higher than normal, usually related to fever • Excess fluid around the tumor site • Some brain related adverse events were commonly experienced only by patients with brain tumors: seizures, partial paralysis (restricted to one side of the body), difficulty walking, falling, confusion, difficulty speaking

UNCOMMON, BUT POTENTIALLY SERIOUS
• Bleeding (including at the tumor site) • Severe Diarrhea • Coughing up blood • Blockage of the main artery of the lung or one of its branches • Blood clot

UNCOMMON, BUT POTENTIALLY SERIOUS
• Opening of a wound along surgical incision • Heart attack or weakening of heart muscle that could result in heart failure • Serious allergic reaction that may result in death. • Stroke (blood clot in brain resulting in nervous system symptoms that may be life-threatening and lead to death) • A tear or a hole in the intestines which may require surgery • Decrease in the level of white blood cells, which may cause greater risk for infection

Risks from Nivolumab

Side effects of nivolumab may happen anytime during treatment or even after your treatment has ended. Some of the common and less common side effects can be serious. **Call or see your healthcare provider right away if you develop any problems listed below or if the symptoms get worse.**

COMMON, SOME MAY BE SERIOUS In 100 people receiving nivolumab, more than 20 and up to 100 may have:
• Tiredness

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving nivolumab, from 4 to 20 may have:
• Anemia which may require blood transfusion • Swelling and redness of the eye • Pain • Diarrhea, nausea • Dry mouth • Fever • Swelling and redness at the site of the medication injection • Bruising, bleeding • Pain or swelling of the joints • Loss of appetite • Reaction during or following a drug infusion which may cause fever, chills, rash • Nivolumab may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Lung problems (pneumonitis and pleural effusion). Symptoms may include: new or worsening cough, chest pain, shortness of breath.
- Intestinal problems (colitis) that can rarely lead to tears or holes in your intestine. Signs and symptoms of colitis may include: diarrhea or increase in bowel movements, blood in your stools or dark, tarry, sticky stools, severe belly pain or tenderness.
- Skin: itching; rash, blisters including inside the mouth; loss of skin pigment
- Liver problems (hepatitis) which can cause liver failure. Signs and symptoms of hepatitis may include: yellowing of your skin or the whites of your eyes, severe nausea or vomiting; drowsiness; pain in the right upper belly
- Hormone gland problems (especially the thyroid, pituitary and adrenal glands, and pancreas). Signs and symptoms may include: headaches that will not go away or unusual headaches, extreme tiredness or changes in mood or behavior; decreased sex drive; weight loss or weight gain; excessive thirst or urine; dizziness or fainting.

RARE, AND SERIOUS

In 100 people receiving nivolumab, 3 or fewer may have:

- Dry eyes
- Sores in the mouth which may cause difficulty swallowing
- Nivolumab may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:
  - Visual disturbances which may cause double vision, blurred vision, or loss of vision with a chance of blindness
  - A condition with high blood sugar which leads to tiredness, frequent urination, excessive thirst, headache, nausea and vomiting, and can result in coma
  - Kidney problems, including nephritis and kidney failure requiring dialysis. Signs of kidney problems may include: decrease in the amount of urine, blood in your urine, ankle swelling.
  - Heart problems including swelling and heart failure. Symptoms and signs of heart problem may include: Shortness of breath, swelling of the ankle and body.
  - Problem of the muscle, including swelling, which can cause muscle pain and severe muscle weakness sometimes with dark urine
  - Swelling of the brain (meningitis/encephalitis) which may cause: headache, stiff neck confusion, sleepiness, seizures or injury to the brain which may cause headache, seizure, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome)
  - Problem of the nerves that can cause paralysis. Signs and symptoms may include: numbness, tingling of hands and feet; weakness of the arms, legs and facial muscle

movement

- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Complications associated with stem cell transplant using donor stem cells (allogeneic stem cell transplant). These complications are caused by attack of donor cells on the host organs (inducing liver, skin and gut damage), and can lead to death. If you are considering an allogeneic stem transplant after participating in this study, please tell your doctor that you have received nivolumab therapy, since the risk and severity of transplant-associated complications may be increased.

Getting medical treatment right away may keep these problems from becoming more serious. Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

Risks from Biopsy

This procedure usually causes only brief discomfort at the site from which the biopsy is taken. Rarely, infection or bleeding may occur at the needle site.

Risks from Sedation

Biopsy will be performed under sedation. Sedation may cause headache, nausea and drowsiness. These side effects usually go away quickly.

Risks from CT scans

If contrast dye is used, there is a risk for allergic reaction to the dye. If you are allergic to or sensitive to medications, contrast dye, iodine, or shellfish, please notify your study doctor. If you have had kidney failure or other kidney problems in the past, please notify your study doctor.

Risk from Electrocardiogram

You may experience some minor skin irritation from the electrodes.

Risks from Blood Collection

Side effects of blood draws include pain and bruising in the area where the needle was placed, lightheadedness, and rarely, fainting. When large amounts of blood are collected, low red blood cell count (anemia) can develop.

What are the risks related to pregnancy?

If you are able to become pregnant, we will ask you to have a pregnancy test before starting this study. You will need to practice an effective form of birth control before starting study treatment, during study treatment, and for 5 months after you finish study treatment (the restricted period). If you become pregnant, there may be unknown risks to the fetus or unborn child, or risks that we did not anticipate. There may be long-term effects of the treatment being studied that could increase the risk of harm to a fetus. You must tell the study doctor if your birth control method fails during the restricted period. If you think or know you have become pregnant during the restricted period, please contact the study team as soon as possible.

If you are a sexually active person with a partner able to become pregnant, it is important that your partner not become pregnant during the restricted period. There may be unknown risks to a fetus or risks we did not anticipate. You and your partner must agree to use birth control if you want to take part in this study. If you think your partner has become pregnant during the restricted period, please contact the study team as soon as possible. If you and your partner plan for your partner to become pregnant after the restricted period, please discuss this with the study team.

What are the risks of radiation from being in the study?

During your participation in this research study, you will be exposed to radiation from CT scans and two CT guided biopsies. The amount of radiation exposure you will receive from these procedures is equal to approximately 9.3 rem. A rem is a unit of absorbed radiation.

Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. The average person in the United States receives a radiation exposure of 0.3 rem per year from these sources. This type of radiation is called "background radiation." This study will expose you to more radiation than you get from everyday background radiation. No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The CT scans that you get in this study will expose you to the roughly the same amount of radiation as 31 years of background radiation. Being exposed to too much radiation can cause harmful side effects such as an increase in the risk of cancer. The risk depends on how much radiation you are exposed to. Please be aware that about 40 out of 100 people (40%) will get cancer during their lifetime, and 20 out of 100 (20%) will die from cancer. The risk of getting cancer from the radiation exposure in this study is 0.9 out of 100 (0.9%) and of getting a fatal cancer is 0.5 out of 100 (0.5%).

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

WHAT ARE THE BENEFITS OF BEING IN THE STUDY?

You might not benefit from being in this study.

However, the potential benefit to you might include shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the cancer.

Are there any potential benefits to others that might result from the study?

In the future, other people might benefit from this study because what we learn in this study may eventually be used to treat others with your disease.

WHAT OTHER OPTIONS ARE THERE FOR YOU?

Before you decide whether to be in this study, we will discuss the other options that are available to you. Instead of being in this study, you could:

- choose to be treated with surgery, radiation or with drugs already approved by the FDA for your disease
- choose to take part in a different study, if one is available
- choose not to be treated for cancer but you may want to receive comfort care to relieve symptoms.

You should discuss with your doctor your other choices and their risks and benefits.

DISCUSSION OF FINDINGS

New information about the study

If we find out any new information that may affect your choice to participate in this study, we will get in touch with you to explain what we have learned. This may be information we have learned while doing this study here at the NIH or information we have learned from other scientists doing similar research in other places.

Return of research results

Results of research studies will not be shared with you.

EARLY WITHDRAWAL FROM THE STUDY

our doctor may decide to stop your therapy for the following reasons:

- if your disease worsens or comes back during treatment
- if you need to take medication that is not allowed on the study
- if you become pregnant
- if you have side effects from the treatment that your doctor thinks are too severe
- if the VB-111 or nivolumab becomes unavailable
- if new information shows that another treatment would be better for you
- if the study is stopped for any reason

In this case, you will be informed of the reason therapy is being stopped.

After the therapy is stopped, we would like to see you for a safety visit approximately one month after stopping therapy.

You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study doctor and your regular doctor first.

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you.

STORAGE, SHARING AND FUTURE RESEARCH USING YOUR SPECIMENS AND DATA

Will Your Specimens or Data Be Saved for Use in Other Research Studies?

As part of this study, we are obtaining specimens and data from you. The specimens will only be used for research in the current study, but leftover specimens may be transferred to the sample collection protocol that we asked you to enroll in. The consent for that describes future research. We plan to use these data collected on the study for studies going on right now, as well as studies in the future. These studies may provide additional information that will be helpful in understanding cancer, or other diseases or conditions. This could include studies to develop other research tests, treatments, drugs, or devices, that may lead to the development of a commercial product by the NIH and/or its research or commercial partners. There are no plans to provide financial compensation to you if this happens. Also, it is unlikely that we will learn anything from these studies that may directly benefit you. By agreeing to let us use your data, you give the NIH any rights you may have in the data.

We may share your data with other researchers. They may be doing research in areas similar to this research or in other unrelated areas. These researchers may be at NIH, other research centers and institutions, or industry sponsors of research.

In addition to the use and sharing of your data described above, we might remove any information from your data, that can identify you such as name, address, or medical record number, and then use your data for additional research studies at the NIH or other places. If we do this, we might not contact you to ask your permission or otherwise inform you.

If you change your mind and do not want us to store and use your data for future research, you should contact the research team member identified at the top of this document. If some research with your data has already been completed, the information from that research may still be used. Also, for example, if the data have been shared already with other researchers, it might not be possible to withdraw the data.

Please place your initials in the blank next to Yes or No for each of the questions below:

My data may be stored and used for future research as described above.

_____ Yes _____ No

Initials Initials

My data may be shared with other researchers and used by these researchers for future research as described above.

_____ Yes _____ No

Initials Initials

How Long Will Your Data be Stored by the NIH?

Your data may be stored by the NIH indefinitely.

Risks of Storage and Sharing of Data

When we store your data, we take precautions to protect your information from others that should not have access to it. When we share your data, we will do everything we can to protect your identity, for example, when appropriate, we remove information that can identify you. Even with the safeguards we put in place, we cannot guarantee that your identity will never become known or someone may gain unauthorized access to your information. New methods may be created in the future that could make it possible to re-identify your specimens and data.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will not receive compensation for participation in this study.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

On this study, the NCI will cover the cost for some of your expenses. Some of these costs may be paid directly by the NIH and some may be reimbursed after you have paid. Someone will work with you to provide more information.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

- If some tests and procedures are performed outside the NIH Clinical Center, you may have to pay for these costs if they are not covered by your insurance company.
- Medicines that are not part of the study treatment will not be provided or paid for by the NIH Clinical Center.
- Once you have completed taking part in the study, medical care will no longer be provided by the NIH Clinical Center.

CONFLICT OF INTEREST (COI)

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a COI Guide. You may ask your research team for a copy of the COI Guide or for more information. Members of the research team who do not work for NIH

are expected to follow these guidelines or the guidelines of their home institution, but they do not need to report their personal finances to the NIH.

The NIH and the research team for this study are using VB-111 developed by VBL Therapeutics through a joint study with your study team and the company. The company also provides financial support for this study.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

A description of this clinical trial will be available on http://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.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database. Your test results will be identified by a unique code and the list that links the code to your name will be kept separate from your sample and health information. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you.

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- The study Sponsor Center for Cancer Research of National Cancer Institute.
- Qualified representatives from VBL Therapeutics, the pharmaceutical company who produces VB-111.

When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

If we share your specimens or data with other researchers, in most circumstances we will remove your identifiers before sharing your specimens and data. You should be aware that there is a slight possibility that someone could figure out the information is about you.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical information that we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Tim Greten, M.D., gretentf@mail.nih.gov, 240-760-6114. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

Please keep a copy of this document in case you want to read it again.

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Legally Authorized Representative (LAR) for an Adult Unable to Consent: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I am legally authorized to make research decisions on behalf of the adult participant unable to consent and have the authority to provide consent to this study. As applicable, the information in the above consent was described to the adult participant unable to consent who agrees to participate in the study.

Signature of LAR	Print Name of LAR	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness to the oral short-form consent process only:

Witness:

Signature of Witness*	Print Name of Witness	Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.