A Phase I Trial of Talimogene Laherparepvec for the Treatment of Peritoneal Surface Malignancies (TEMPO)

Trial: NCT03663712

Consent Forms for

Duke University (October 28, 2022)

University of Illinois at Chicago (January 5, 2022)

Wake Forest University (December 12, 2022)

DUKE UNIVERSITY HEALTH SYSTEM

Consent to Participate in a Research Study

A Phase I Trial of Talimogene Laherparepvec (TVEC) for the Treatment of Peritoneal Surface Malignancies (TEMPO)

PI: Dan Blazer III, MD

CONCISE SUMMARY

This is a research study to find what effects, good and/or bad, an investigational drug called Talimogene Laherparepvec (TVEC) has on you and your cancer. We hope TVEC will actively kill tumor cells and promote your own body's immune system to attack your tumor as well. If proven effective, TVEC may be developed into a new therapeutic approach for treating human peritoneal surface dissemination of gastrointestinal and ovarian cancers.

TVEC will be administered via peritoneal catheter on Day 1 and 22 of the first 5-week cycle. Each subsequent cycle will be 2 weeks long, and the study drug will be administered on day 1 of each cycle. The study drug infusions will end after the completion of cycle 4. You will have tests, exams, and procedures that are part of your standard care and for study purposes.

There are risks to this study drug that are described in this document. Some risks include: flu like illness, injection site pain, joint pain, headache, arm or leg pain, and diarrhea. There may be some unknown but potentially serious and life-threatening side effects.

If you are interested in learning more about this study, please continue reading below.

You are being asked to take part in this research study because you have stage IV peritoneal surface dissemination of gastrointestinal, fallopian tube, ovarian, or primary peritoneal cancer (peritoneal carcinomatosis). Research studies are voluntary and include only people who choose to take part. Please read this consent form carefully and take your time making your decision. As your study doctor or study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. We encourage you to talk with your family and friends before you decide to take part in this research study. The nature of the study, risks, inconveniences, discomforts, and other important information about the study are listed below.

Please tell the study doctor or study staff if you are taking part in another research study.

Dr. Dan Blazer III will conduct the study and it is funded by Amgen. The sponsor of this study, Amgen, will pay Duke University to perform this research, and these funds may reimburse part of Dr. Blazer's salary. Dr. Strickler has received personal compensation from Amgen for speaking and advisory board work. Dr. Strickler may receive personal compensation from the sponsor in the future.

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WHO WILL BE MY DOCTOR ON THIS STUDY?
If you decide to participate, Dr. Blazer or another study physician will be your doctor for the study and will be in contact with your regular health care provider throughout the time that you are in the study and afterwards, if needed.

WHY IS THIS STUDY BEING DONE?
The purpose of this study is to find out what effects, good and/or bad, Talimogene Laherparepvec (TVEC) has on you and your cancer.

HOW DOES THIS DRUG WORK?
TVEC is a drug that will be given in your abdomen that is an oncolytic virus. This means that it is a genetically modified version of the herpes virus that is designed to reproduce in tumor tissue and stimulate your immune system to attack the tumor cells. TVEC is FDA approved for treatment of individual lesions in patients with metastatic melanoma, but is considered investigational in peritoneal carcinomatosis. The word "investigational" means that the study drug is being tested in research studies and is not approved by the U.S. Food and Drug Administration (FDA) for this use.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?
Approximately 45 people will take part in this study at Duke Cancer Institute, University of Illinois Cancer Center, and Wake Forest University. This includes 11 to 34 subjects in the Dose Escalation Cohort and 11 subjects in the Dose Expansion Cohort.

WHAT IS INVOLVED IN THE STUDY?
Screening:
If you agree to be in this study, you will be asked to sign and date this consent form. You will have the following tests and procedures to make sure that you are eligible to participate and to ensure that the study drug does not pose a special risk to you:

- Physical exam and medical history
- Demographics (information such as your gender, race, age, etc)
- List of medications that you are taking
- Vital signs (temperature, blood pressure, heart rate, and weight)
- CT scans or MRI scans for tumor measurement
- Blood tests will be taken for the following:
    - Routine blood tests – these tests will evaluate blood cell counts, blood chemistry, liver and kidney function, and how well your blood clots.
    - Blood tumor markers – this test can indicate whether your tumor is responding to the study drug.

- Pharmacogenomics – this test will help indicate how your genes affect your response to the study drug.
- If you are a woman able to bear children, you will also have a small blood sample taken for a pregnancy test. Pregnant women are not eligible to participate in this study.

Peritoneal Catheter Placement

After you are determined to meet eligibility for this study, you will have a catheter placed within 2 to 6 days prior to starting treatment. This catheter is a small flexible tube that will be inserted into the wall of your abdomen to allow the study drug to be put in.

Study Drugs

If the exams, tests, and procedures show that you can be in the study, and you choose to take part, you will be enrolled in the study.

On the first day of the study drug infusion, the planned dose of TVEC will be delivered via the peritoneal catheter in 500 mL of normal saline. After the infusion, you will roll onto your right side, wait 10 minutes, then roll to the left side and wait an additional 10 minutes, and repeat this procedure of rolling to the right side and the left side every 10-15 minutes for one hour. Then, you will be observed for an additional hour to make sure you tolerated the study drug infusion well.

You will have study drug infusion as described above on Day 1 and 22 of the first 5-week cycle. Each subsequent cycle will be 2 weeks long, and study drug will be administered on day 1 of each cycle. Study drug infusion will end after the completion of cycle 4.

For your safety, you will be monitored to be sure any side effects are prevented or minimized. This will require regular clinic visits, blood and urine tests, and radiology tests. These tests to check you and your cancer are part of your routine care. You will continue to receive study drug until the end of cycle 4, or if you experience excessive side effects or choose to withdraw from the study.

Assessments During Drug Regimen:

Day 1 of Cycle 1

- Physical examination
- Vital signs (every 10-15 minutes for one hour, then again after an additional hour of observation)
- List of your medications
- Routine blood tests, including blood cell count and blood chemistry (prior to study drug infusion)
- Urine pregnancy test prior to study drug infusion (Only for women of childbearing potential)

- Viral load – blood and urine tests that measure the amount of the TVEC virus present in your body (done prior to study drug infusion)
- Viral antibody titers – blood test used to help measure how many antibodies your body is producing in response to TVEC (prior to study drug infusion)
- Peritoneal cytokines – some fluid from your peritoneal catheter will be used to help measure how your immune system is responding to the study drug (prior to study drug infusion)
- Plasma for protein multiplex arrays – blood test to measure how your immune system is responding to the study drug (prior to study drug infusion)
- Immune cells – blood and some fluid from your peritoneal catheter will be collected to help measure how your immune system is responding to the study drug (prior to study drug infusion)
- TVEC administration

Day 22 of Cycle 1

- Physical examination
- Vital signs (every 10-15 minutes for one hour, then again after an additional hour of observation)
- List of your medications
- Routine blood tests, including blood cell count and blood chemistry (prior to study drug infusion)
- Urine pregnancy test prior to study drug infusion (Only for women of childbearing potential)
- Viral load (prior to study drug infusion)
- Viral antibody titers (prior to study drug infusion)
- Plasma for protein multiplex arrays (prior to study drug infusion)
- TVEC administration

Days 8, 15, and 28 of Cycle 1

- Physical examination
- Vital signs
- List of your medications
- Routine blood tests, including blood cell count and blood chemistry
- Viral load

Day 1 of Cycles 2, 3, and 4

- Physical examination
- Vital signs (every 10-15 minutes for one hour, then again after an additional hour of observation)
- Routine blood tests, including blood cell count and blood chemistry
- Urine pregnancy test prior to study drug infusion (Only for women of childbearing potential)
- Viral load (prior to study drug infusion)

- Peritoneal cytokines (prior to study drug infusion, not done on Cycle 3 Day 1)
- Immune cells (prior to study drug infusion, not done on Cycle 3 Day 1)
- Plasma for protein multiplex arrays (prior to study drug infusion)
- TVEC administration

Day 14 of Cycle 4

- CT scans or MRI scans for tumor measurement
- Blood tumor markers

30 Days (+/-7 Days) After Final Dose

- Physical examination
- Vital signs
- Routine blood tests, including blood cell count and blood chemistry
- Pregnancy test (women of childbearing potential only)
- Viral load
- Peritoneal cytokines
- Immune cells
- Plasma for protein multiplex arrays
- Study nurse will follow up with you every 12 weeks until your disease progresses or you start new anti-cancer therapy
- Tumor tissue – archived tumor from your primary diagnosis will be collected at the end of the study

<u>Optional Consent for use of Leftover Samples for Future Biomarker Research</u>

With your permission, your blood and/or tissue samples may be shared anonymously with other investigators for research purposes. The samples may be used for study of disorders unrelated to the one(s) in your family. Such research will be strictly anonymous, in that no identifying information that would link the samples to you is provided to the researcher. An ethics board will review any such research prior to access being given to your samples. This secondary use will in no way compromise the study of the disorder(s) in your family or the use of your samples as part of this study.

Tissue, blood, or other samples collected as part of this study may be valuable for scientific, research, or teaching purposes or for the development of a new medical or commercial product. DUHS and/or the developers will assert all rights of ownership in the samples and all rights arising from use of the samples. There is no plan to compensate you for any use of the samples.

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Please indicate below whether or not you wish to provide your consent to take part in this optional research.

I agree to provide an additional blood sample for the research described above.

☐ Yes ☐ No Please initial here: _____ Date: _____

Participation in Genetic Studies

The genetic studies described are for research purposes only. Therefore, you will receive no results from this study (except as described above and in this section). It is not the purpose of this study to look for or provide you with any medical information or diagnoses relating to your present condition or any other disease or illness. The research tests are not being used as diagnostic tests for any disease or illness. Your participation in this study is not a substitute for your regular medical care or check-ups.

Through this research, we may find that you have an abnormal gene or gene product (RNA or protein) which indicates a risk for developing a disease at some time in the future. It is also possible that the research results may indirectly provide unexpected personal information about you or your family (such as ethnic/racial background or an unknown genetic relationship between family members). Please talk with the study doctor if you have any questions or concerns about the genetic testing being done in this research study. He/she may also refer you to a genetic counselor for further information.

It is possible that this study will identify information about you that was previously unknown, such as disease status or risk. There are no plans to provide this information to you or your physician.

HOW LONG WILL I BE IN THIS STUDY?

You will be asked to remain in the study from the screening period until your 30 day follow up visit, which is a total of 5 months. We would like to keep track of your medical condition for up to two years. Keeping in touch with you and checking on your condition helps us look at the long-term effects of the study.

You can choose to stop participating at any time without penalty or loss of any benefits to which you are entitled. However, if you decide to stop participating in the study, we encourage you to talk to your doctor first.

It is important to tell the study doctor if you are thinking about stopping so any risks from the study drugs can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you. The study doctor

may stop you from taking part in this study at any time if she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

WHAT ARE THE RISKS OF THE STUDY?

Drugs used for anti-cancer therapy often have some undesirable side effects. It is important to be aware that there may be other side effects that are not yet known and cannot be foreseen. Side effects may go away after the study drug has stopped, but it is also possible that side effects may last a long time or forever. They may range from mild to life threatening or even lethal. It is possible that side effects can be minimized with additional treatments. Many side effects can be prevented or minimized by noticing the side effects early while they are still mild. Therefore, it is important to tell the study doctor or study nurse immediately about any changes in health that may have occurred even if you do not think they are related to the study. Your study doctor may give you treatment to help control side effects. If your study nurse or study doctor explains how to apply some preventative measures (for example to reduce risk of skin toxicity) please listen carefully. As a result of your participation in this study, you are at risk for the following side effects. You should discuss these with the study doctor and your regular health care provider if you choose.

As of 26 October 2021, more than 7,416 people have received talimogene laherparepvec with approximately 1,479 subjects having received talimogene laherparepvec in research studies and approximately 5,937 patients were prescribed talimogene laherparepvec (IMLYGIC®) after it was approved for sale.

Side effects that other people have had in research studies that are thought to have been caused by talimogene laherparepvec are:

Very Common Side Effects ***(may affect more than 1 person in 10)***

- Flu like illness: chills, fever, feeling tired, muscle pain, nausea and vomiting
- Injection site pain
- Headache
- Joint pain
- Arm or leg pain
- Diarrhea
- Constipation

Common Side Effects ***(may affect between 1 and 10 people in every 100)***

- Injection site reactions: bleeding, redness, swelling, inflammation

- Skin infection caused by bacteria at the site of injection: symptoms may include fever, chills, redness or swelling at the injection site or the site of the tumor, and may require hospitalization for antibiotic treatment
- Wound complication at the injection site (secretion or discharge)
- Pain: pain after procedure, in the tumor, in the abdomen, throat pain, pain in the armpit or groin
- Abdominal discomfort
- Cold sore or fever blister in mouth (Oral herpes)
- Low red blood cell count (Anemia)
- Not feeling well (Malaise)
- Weight loss
- Dehydration
- Bruise
- Dizziness
- Skin or face becomes warm and reddened (Flushing)
- Rash
- Inflamed skin (Dermatitis)
- Blood clot (Deep vein thrombosis)
- Autoimmune Reactions: (a reaction of your body's immune system fighting your body's own tissues) have been reported in some patients administered talimogene laherparepvec. Examples of autoimmune reactions that have been reported in patients receiving talimogene laherparepvec include:
    - Inflammation of the kidneys (glomerulonephritis)
    - Inflammation of the blood vessels (vasculitis)
    - Inflammation of the lungs (pneumonitis)
    - Areas of skin with loss of color (vitiligo)
    - If you already have psoriasis (itchy, flaky patches or scaling of the skin), it may get worse

  It is possible that an autoimmune reaction could occur in any part of the body. Please tell your doctor if you have had any type of autoimmune disease before administration of talimogene laherparepvec, and all treatments you are receiving for the disease.

<u>Uncommon Side Effects</u> ***(which may affect between 1 and 10 people in every 1000)***

- Injection site reactions: warmth, incision site infection
- Eye infection caused by herpes virus (Herpetic keratitis)

- Difficulty breathing: People receiving talimogene laherparepvec have experienced difficulty breathing or the sensation of shortness of breath. In addition, if you have a tumor in your neck, your doctor may warn you that you might experience compression of your airways while receiving talimogene laherparepvec. This might require a surgical procedure on the neck to open a direct airway. This occurred in a talimogene laherparepvec treated patient who had a similar problem before treatment. A tube might need to be inserted into the opening in your throat. This tube may be connected to a machine to help you breathe.
- Plasmacytoma (a collection of abnormal antibody-producing white blood cells) in the area where talimogene laherparepvec is injected. Plasmacytoma may be associated with multiple myeloma (a cancer of white blood cells affecting the bone marrow).
- Symptoms of delayed wound healing at or around the injection site such as injection site discharge, foul odor, or dead tissue at the injection site. If you notice symptoms of delayed wound healing at the injection site(s), especially if you have risk factors such as diabetes, poor blood circulation, have had radiation to the site, you should contact the study doctor or his/her study staff immediately.

Injection Site Reactions – Reactions at or near the area of the injection have been seen in other people administered talimogene laherparepvec. Symptoms include bleeding, redness, swelling and inflammation of the injection site. Skin infection caused by bacteria at the site of injection which may require hospitalization for antibiotic treatment have also been reported. Other symptoms may include warmth at the injection site or symptoms of delayed wound healing at or around the injection site such as injection site discharge, foul odor, or dead tissue at the injection site. If you notice symptoms of delayed wound healing at the injection site(s), you should contact the study doctor or his/her staff immediately.

Side Effects with Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF) – Talimogene laherparepvec contains genetic material that makes human GM-CSF. Human GM-CSF is a medicine used to treat patients with blood cell counts that are all low. Known side effects of human GM-CSF include, but are not limited to, musculoskeletal pain, fever, chills, shortness of breath, rash, fatigue, gastrointestinal effects, and fluid around heart and lungs. Although the amount of human GM-CSF released when treating tumor lesions with talimogene laherparepvec is very small, these side effects may still occur and your doctor will be looking for them.

Transmission of Talimogene Laherparepvec – You should always observe proper hygiene (wash your hands with warm water and soap after touching your injected lesions or injected sites or handling the dressings) to avoid potentially spreading talimogene laherparepvec to other persons.

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Herpetic infections have been reported in close contacts or family members of subjects receiving talimogene laherparepvec. TVEC could potentially spread to your family members or other close contacts (household members, care-givers, sex partners, or someone you share a bed with) at any time after your tumor(s) are injected with the study drug. This may occur if your family member or other close contact touches the injection site or has contact with your body fluids or with the inside of the dressing(s) covering your injection site(s).

Spreading TVEC may be more likely if your close contact has a break in the skin or mucous membranes that comes into contact with your injection site or your body fluids. In patients treated with TVEC in clinical trials, TVEC has been found on the surface of the injected tumors, and on the outside of the dressings that covered these injection sites.

Talimogene laherparepvec have also been detected in patients' blood and urine, and in the patient's mucous membranes of the mouth and genitals, no samples had detectable talimogene laherparepvec 30 days after the end of treatment. For patients who had talimogene laherparepvec presence in the surface of injected tumors, no samples had detectable talimogene laherparepvec 60 days after end of treatment.

If a close contact has been exposed to TVEC, it is possible that they could develop symptoms similar to that of a herpes virus infection (see below). However, the chance of this happening is low due to the changes in TVEC that make it different from the naturally occurring herpes simplex virus, but you should know how to recognize these symptoms. Please contact the study doctor or study staff if a close contact develops herpes virus infection symptoms.

Most adults in the population have been exposed to the naturally occurring herpes simplex (also known as "cold sore") virus (HSV-1). Common signs and symptoms of the naturally occurring herpes simplex virus include:

- Sores around the mouth ("cold sore", "fever blister") or the genitals ("genital sore").
- Blisters may develop on the fingers, ears, or face.
- Eye infection (herpetic keratitis) with eye pain, light sensitivity, discharge from the eyes or blurry vision.
- Abdominal pain and infections, and inflammation inside the abdomen (infrequently).
- Rarely, serious infections of the brain (encephalitis) or spinal cord, causing paralysis (unable to move) have been reported. Signs may include fever, confusion or other behavior changes, headache, numbness and pain in the legs, constipation, or difficulty with urination.

- Life-threatening infections (disseminated herpes) can develop in people with a weakened immune system.
  - Disseminated herpes is a type of herpes infection that has spread to other parts of the skin and internal organs.

After infection, the naturally occurring herpes virus may travel to spinal nerve roots. The virus can reactivate from the nerve roots and cause recurrent cold sores or other signs of infection as described above. Stress, other illness, or menstruation are common triggers for reactivation of the naturally occurring virus.

Signs and symptoms of infection with TVEC could be similar to those described above, although TVEC has been changed to reduce the chance of this happening.

Delay in Response with TVEC Administration – Given that TVEC may help by stimulating your immune system (immunotherapy), it is possible that there can be a delay in your body responding to the study drug. In addition, you may also see an increase in the size of existing tumors and/or the development of new tumors before potentially seeing a response to TVEC.

Allergic Reactions – As with any medication, you may have an allergic reaction to TVEC. Symptoms of an allergic reaction in general may include headache, rash, itching, flushing, swelling, shortness of breath, nausea and sometimes vomiting. Severe allergic reactions can cause dizziness, severe skin reactions, difficulty breathing or swallowing, a decrease in blood pressure, and could be life threatening. If you have symptoms of an allergic reaction, you should contact the study doctor or his/her study staff immediately. If you have had an allergic reaction to TVEC or any of its ingredients, you should inform your doctor.

Reproductive Risks

For women: The effects of the study drug on a developing pregnancy are not well understood, although herpes viruses are known to cause complications during pregnancy. Women who are pregnant or breastfeeding are excluded from this study.

If you are a woman who could possibly become pregnant (you have not completed menopause, or you have not had a hysterectomy and/or both tubes and/or both ovaries removed), and you have a partner who is able to father children, a blood pregnancy test will be done (using 1 teaspoon of blood drawn from a vein by needle-stick), and it must be negative before you can continue in this study. In women 40 years old and older, blood pregnancy tests can sometimes give a false positive or indeterminate result, and additional testing may be required.

You and your partner must agree to either abstain completely from vaginal intercourse for the duration of this study and for 90 days after the last dose of study drug, or agree to use highly effective methods of contraception for the same length of time. Highly effective methods include (a) partner vasectomy, (b) bilateral tubal ligation, (c) intrauterine devices (IUDs), (d) hormonal implants (e.g., Implanon), (e) other hormonal methods (birth control pills, injections, patches, vaginal rings) plus a barrier method (condoms, diaphragms, cervical caps) plus spermicide, or (f) condoms plus a diaphragm or cervical cap plus spermicide. If you are not currently using one of these methods, your study doctor will discuss options with you, given your medical condition, your personal preferences, and the level of protection required by this study. Because no birth control method is 100% effective, you should contact your study doctor immediately if you think there is any chance you could be pregnant.

For men: The effects of the study drug on a developing pregnancy that began while the father was taking the drug are unknown, and the study drug may be present in semen and transmitted to a partner during sexual activity. If you have a partner who could possibly become pregnant (she has not completed menopause, or she has not had a hysterectomy and/or both tubes and/or both ovaries removed), you must agree to either abstain completely from vaginal intercourse for the duration of the study and for 90 days after the last dose of study drug, or use a condom every time you have intercourse for the same length of time. This is true even if you have had a vasectomy (since vasectomy does not prevent transmission in semen). If your partner is currently pregnant or breastfeeding, you must use a condom for all types of intercourse. You should inform your partner about the potential risks of the study drug. If she is not currently using another method of contraception, she should consider discussing options with her health care provider. If she does become pregnant during your participation in the study, you will need to report it to the study doctor, and she should promptly notify her doctor.

Risks of Peritoneal Catheter:

There are several risks associated with the use of a peritoneal catheter.

The risk of **bowel perforation** is less than 1% (meaning it happens to fewer than 1 in 100 people), and it usually occurs during entry into the abdominal cavity or when the catheter and stylet (probe) are moved further into the abdomen. Surgical exploration is necessary with repair of the perforation and removal of the catheter.

Bleeding is rarely a significant problem after peritoneal catheter placement. This typically does not require medical intervention outside of holding pressure at the exit site.

Wound infection is uncommon and often can be treated with antibiotics when it is on the surface. If the wound is deeper, then it may need to be drained surgically.

Outflow failure may be due to several causes including clots or fibrin (protein) in the catheter, a kink in the tunnel under the skin, placement of the catheter in the omentum (organ above the intestines), blockage from omentum, or adhesions (scar-like tissues). A number of treatments might be required including flushing with a clot dissolving agent and repositioning of the catheter.

Leakage of the infusion solution may be identified by the presence of drainage at the exit site or the appearance of a bulge underneath the catheter site. An x-ray study of the catheter will determine the method of treatment that is pursued.

Risks of Peritoneal Catheter – TVEC Administration:
In this study, TVEC will be administered into the peritoneum via intraperitoneal catheter. Since this administration method is different than the approved method of administering the drug normally, there may be additional associated risks. These include:

Ileus (the inability of the intestine (bowel) to contract normally and move waste out of the body)
Bowel perforation (rupture) due to tumor response
Peritonitis (inflammation of the membrane lining the abdominal wall and covering the abdominal organs)

Risks of Drawing Blood:
Risks associated with drawing blood from your arm include momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or fainting are also possible, although unlikely.

Risk of CT Scan:
Computed Tomography (CT) is a way to make x-ray images of the inside of the body. The CT scanner is a doughnut-shaped machine that uses x-rays to create computer pictures that show structures inside your body more clearly than regular x-ray pictures. During the procedure, a technologist will take you into the CT scan room where you will lie down on the subject table (usually on your back) inside of the CT machine. You should get comfortable because it is very important that you not move during certain parts of the test.

CT examinations differ depending on the part of your body being studied. For example, if your abdomen is being studied, a series of pictures will be taken from your lower chest to your lower pelvis. During the study, you will be asked to hold your breath so that the pictures will not be blurred. The machine will make some noise, and the table will move during the scan. Also, you may receive signals from the

technologist or from the machine about your breathing. Before or during the study, you may be given an injection of contrast liquid in your vein to allow the radiologist to obtain clearer images of your organs. If you have any discomfort during the test or after the injection, be sure to tell the technologist.

Risk of MRI Scan:
Magnetic resonance imaging (MRI) uses a magnet and radio waves to make diagnostic medical images of the body. There have been no ill effects reported from exposure to the magnetism or radio waves used in this test. However, it is possible that harmful effects could be recognized in the future. A known risk is that the magnet could attract certain kinds of metal. Therefore, we will carefully ask you about metal within your body (this includes certain dyes found in tattoos). If there is any question about potentially hazardous metal within your body, you will not be able to have an MRI.

If you have an MRI as part of your tumor assessment, you will enter a large room in which a magnet is present. You will be placed on a narrow bed and then slide into a small tunnel approximately 6 feet in length and 25 inches in diameter. You will be asked to lie still for about one hour on this bed. You will hear a loud machine-like noise. You may be asked to have a harmless monitoring device applied during the study. During the study, you can have voice contact and physical contact with someone in attendance if you desire.

Risks of Radiation:
You will have a number of CT scans or MRI scans that are part of the regular care for your condition, and you would have them whether or not you participate in this research. These studies will not add to the risk due to participating in the research. However, if you have concerns about the overall radiation exposure or MRI safety issue, you should discuss them with your physician.

Sometimes subjects have allergic reactions to the dyes used in imaging scans. This is rare. It can involve itching or rash. In severe cases, you may have difficulty breathing and dangerous lowering of your blood pressure. If you know that you have an allergy to the dye, or to iodine or shellfish, please let your study doctor and radiologist know.

Drug and Food Interactions:
For your safety, you must tell the study doctor or nurse about all the prescribed medical foods and drugs, herbal products, over-the-counter (OTC) drugs, vitamins, natural remedies, and alcohol that you are taking before you start the study and before starting to take any of these products while you are on the study.

Potential Risks of Genetic Testing and the Genetic Information Non-Discrimination Act (GINA):
There is a potential risk of loss of confidentiality. Every effort will be made to protect your confidential

information, but this cannot be guaranteed. The genetic information obtained as a result of your participation in this research will not be included in your medical record. Information from which you may be personally identified will be maintained in a confidential, secure location at DUHS, accessible only by authorized members of the study team, and you will not be disclosed to third parties except as described in this consent form, with your permission, or as may be required by law.

The Genetic Information Nondiscrimination Act (GINA) is a Federal law that will protect you in the following ways:
-Health insurance companies and group plans may not request genetic information from this research
-Health insurance companies and group 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 when making a decision to hire, promote, or fire you or when setting the terms of your employment.

GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

There may be risks, discomforts, drug interactions or side effects that are not yet known.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?
If you agree to take part in this study, the investigational study drug may help control your cancer. This may or may not make you feel better or live longer. We hope that in the future the information learned from this study will benefit other people with your condition. If proven effective, TVEC may be developed into a new therapeutic approach for treating human peritoneal surface dissemination of gastrointestinal and ovarian cancers.

WHAT ALTERNATIVES ARE THERE TO PARTICIPATION IN THIS STUDY?
Your other choices may include the following:

- Getting treatment or care for your cancer without being in a study
- Depending on the therapies that you have already received, there may be other potentially beneficial approved treatments available for your cancer. These treatments may shrink tumors, delay progression of cancer, provide symptom relief, or prolong your life and could include chemotherapy (for example, platinum-based chemotherapy) or drugs that target a specific abnormality in some cancers. You should discuss these options with your doctor.
- Taking part in another study.
- Getting no treatment

- Getting comfort care (also called palliative care) only. This type of care helps reduce pain, tiredness, appetite problems, and other problems caused by the cancer. It does not treat the cancer directly.

Talk to your doctor about your choices, including the risks and benefits of each choice, before you decide if you will take part in this study.

WILL MY INFORMATION BE KEPT CONFIDENTIAL?

Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total confidentiality. Your personal information may be viewed by individuals involved in this research and may be seen by people including those collaborating, funding, and regulating the study. We will share only the minimum necessary information in order to conduct the research. Your personal information may also be given out if required by law.

As part of the study, results of your study-related laboratory tests, x-rays, and procedures may be reported to Amgen and its affiliates. In addition, your records may be reviewed in order to meet federal or state regulations. Reviewers may include representatives from the Food and Drug Administration, representatives and affiliates of Amgen, the Duke Cancer Institute, the Duke Office of Audit, Risk, and Compliance, the Duke University Health System Institutional Review Board, and others as appropriate. If any of these groups review your research record, they may also need to review your entire medical record.

As part of this study, you will be asked to have certain tests, x-rays, and/or procedures performed. Some of these tests, x-rays and/or procedures would have been done as part of your regular care. The study doctor will use these test results both to treat you and to complete this research. These test results will be recorded in your medical record and will be reported to the representatives and affiliates of Amgen. Results of tests and studies done solely for this research study and not as part of your regular care will not be included in your medical record.

The study results will be retained in your research record for at least six years after the study is completed. At that time either the research information not already in your medical record may be destroyed or information identifying you will be removed from such study results at DUHS. Any research information in your medical record will be kept indefinitely.

This information may be further disclosed by the sponsor of this study. If disclosed by the sponsor, the information is no longer covered by federal privacy regulations.

DUKE UNIVERSITY HEALTH SYSTEM

Consent to Participate in a Research Study

A Phase I Trial of Talimogene Laherparepvec (TVEC) for the Treatment of Peritoneal Surface Malignancies (TEMPO)

PI: Dan Blazer III, MD

If this information is disclosed to outside reviewers for audit purposes, it may be further disclosed by them and may not be covered by federal privacy regulations.

While the information and data resulting from this study may be presented at scientific meetings or published in a scientific journal, your name or other personal information will not be revealed.

Some people or groups who receive your health information might not have to follow the same privacy rules. Once your information is shared outside of DUHS, we cannot guarantee that it will remain private. If you decide to share private information with anyone not involved in the study, the federal law designed to protect your health information privacy may no longer apply to the information you have shared. Other laws may or may not protect sharing of private health information.

WHAT ARE THE COSTS TO YOU?
You or your insurance provider will be responsible and billed for all costs related to your routine medical care, including copayments and deductibles. Routine medical care services are those that you would have received for your condition if you were not participating in this research study. Not all services are covered by insurance. Some procedures or scans may require pre-authorization by your insurance plan. We will notify you if we learn that a service is not covered by your insurance plan as part of the pre-authorization process. If it is not covered, you will be responsible for paying for it. The amount of your out-of-pocket expense will depend on your insurance plan. For beneficiaries with Medicare Advantage Plans, traditional Medicare is billed for the routine cost of a research study. You may have more or higher co-pays than with a Medicare Advantage plan. Please discuss the costs of the study with Dr. Stewart. At your request, a Financial Counselor in the clinic may provide you with an estimate of costs for routine services.

The study sponsor Amgen has agreed to pay for services and procedures that are done solely for research purposes. Please talk with the PI/study team about the specific services and procedures that the sponsor will pay for, and the ones for which you or your insurance will be responsible.

We will monitor your DUHS patient care charges to make sure that costs are directed appropriately. If you have any questions or concerns about appropriate billing, contact your study team coordinator so that he/she can help find a resolution.

Amgen will provide the study drug free of charge to you.

WHAT ABOUT COMPENSATION?
You will not receive any monetary compensation for your participation in this study.

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WHAT ABOUT RESEARCH RELATED INJURIES?
Immediate necessary medical care is available at Duke University Medical Center in the event that you are injured as a result of your participation in this research study. However, there is no commitment by Duke University, Duke University Health System, Inc., your Duke physicians, or the study supporter, Amgen, Inc., to provide monetary compensation or free medical care to you in the event of a study-related injury.

For questions about the study or research-related injury, contact Dr. Blazer at 919-668-1861 during regular business hours. After hours and on weekends and holidays, please call the Duke paging operator at 919-684-8111, and ask the operator to page Dr. Blazer.

WHAT ABOUT MY RIGHTS TO DECLINE PARTICIPATION OR WITHDRAW FROM THE STUDY?
You may choose not to be in the study, or, if you agree to be in the study, you may withdraw from the study at any time. If you withdraw from the study, no new data about you will be collected for study purposes unless the data concern an adverse event (a bad effect) related to the study. If such an adverse event occurs, we may need to review your entire medical record. All data that have already been collected for study purposes, and any new information about an adverse event related to the study, will be sent to the study sponsor.

Your decision not to participate or to withdraw from the study will not involve any penalty or loss of benefits to which you are entitled, and will not affect your access to health care at Duke. If you do decide to withdraw, we ask that you contact Dr. Blazer in writing and let him know that you are withdrawing from the study. His mailing address is:

c/o Protocol Office
Box 3233
DUMC
Durham, NC 27710

Dr. Blazer may ask you to return for a checkup before you stop your study drug if he thinks that stopping the drug suddenly may harm you. He may also ask you to complete the tests that would ordinarily occur when a person completes the study.

We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

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Your doctor may decide to take you off this study if your condition gets worse, if you have serious side effects, or if your study doctor determines that it is no longer in your best interest to continue. The sponsor or regulatory agencies may stop this study at anytime without your consent (reasons may include unanticipated drug toxicity or lack of effectiveness). If this occurs, you will be notified and your study doctor will discuss other options with you.

If you agree to allow your tissue to be kept for future research with identifying information that could link your sample to you, you are free to change your mind at any time. We ask that you contact Dr. Blazer in writing and let him know you are withdrawing your permission for your identifiable tissue to be used for future research. His mailing address is above. At that time we will ask you to indicate in writing if you want the unused identifiable tissue destroyed or if your samples (having all identifying information removed that would link the sample to you) could be used for other research.

Your samples and/or data may be stored and shared for future research without additional informed consent if identifiable private information, such as your name and medical record number, are removed. If your identifying information is removed from your samples or data, we will no longer be able to identify and destroy them.

The use of your samples may result in commercial profit. You will not be compensated for the use of your samples other than what is described in this consent form.

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

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or a research-related injury, or if you have problems, concerns, questions or suggestions about the research, contact Dr. Blazer at (919) 668-1861 during regular business hours and at (919) 684-8111 after hours and on weekends and holidays and ask that he be paged.

For questions about your rights as a research participant, or to discuss problems, concerns or suggestions related to the research, or to obtain information or offer input about the research, contact the Duke University Health System Institutional Review Board (IRB) Office at (919) 668-5111.

DUKE UNIVERSITY HEALTH SYSTEM

Consent to Participate in a Research Study

A Phase I Trial of Talimogene Laherparepvec (TVEC) for the Treatment of Peritoneal Surface Malignancies (TEMPO)

PI: Dan Blazer III, MD

STATEMENT OF CONSENT

"The purpose of this study, procedures to be followed, risks and benefits have been explained to me. I have been allowed to ask questions, and my questions have been answered to my satisfaction. I have been told whom to contact if I have questions, to discuss problems, concerns, or suggestions related to the research, or to obtain information or offer input about the research. I have read this consent form and agree to be in this study, with the understanding that I may withdraw at any time. I have been told that I will be given a signed and dated copy of this consent form."

_____
Printed name of Subject

_____ _____ _____
Signature of Subject Date Time

_____
Printed name of Person obtaining consent

_____ _____ _____
Signature of Person Obtaining Consent Date Time

University of Illinois at Chicago
Research Information and Consent for Participation in Biomedical Research
A Phase I Trial of Talimogene Laherparepvec (TVEC) for the Treatment of Peritoneal Surface Malignancies (TEMPO)

Principal Investigator/Researcher Name and Title: Shannon MacLaughlan, MD

Department and Institution: University of Illinois, Division of Gynecologic Oncology

Address and Contact Information: Department of Obstetrics and Gynecology
840 S. Wood St. 263 CSN MC 808
Chicago, Il 60612
Phone: 312-413-9874

Sponsor: Dan Blazer III, MD at Duke University Medical Center, Financial support by Amgen

About this research study
You are being asked to participate in a research study. Research studies answer important questions that might help change or improve the way we do things in the future.

Taking part in this study is voluntary
Your participation in this research study is voluntary. You may choose to not take part in this study or may choose to leave the study at any time. Deciding not to participate, or deciding to leave the study later, will not result in any penalty or loss of benefits to which you are entitled and will not affect your relationship with the University of Illinois Hospital and Health Sciences System (UI Health) and/or University of Illinois at Chicago (UIC).

This consent form will give you information about the research study to help you decide whether you want to participate. Please read this form and ask any questions you have before agreeing to be in the study.

Important Information
This information gives you an overview of the research. More information about these topics may be found in the pages that follow.

Note: This research includes subjects who are adults who are not able to consent for themselves. If you are a parent, guardian, or legal representative, the terms "you" or "your" refer to the research subject.

WHY IS THIS STUDY BEING DONE?	This is a research study to find what effects, good and/or bad, an investigational drug called Talimogene Laherparepvec (TVEC) has on you and your cancer. We hope TVEC will actively kill tumor cells and promote your own body's immune system to attack your tumor as well. If proven effective, TVEC may be developed into a new therapeutic approach for treating human peritoneal surface dissemination of gastrointestinal, fallopian tube, ovarian or primary peritoneal cancers.
WHAT WILL HAPPEN TO ME DURING THE STUDY?	TVEC will be administered via peritoneal catheter on Day 1 and 21 of the first 5-week cycle. Each subsequent cycle will be 2 weeks long, and study treatment will be administered on day 1 of each cycle. Study treatment will end after the completion of cycle 4. You will have tests, exams, and procedures that are part of your standard care and for study purposes. For more information, please see the "What Procedures Are Involved?" section below.
HOW MUCH TIME WILL I SPEND ON THE STUDY?	You will be asked to remain in the study from the screening period until your 30 day follow up visit, which is a total of 5 months. We would like to keep track of your medical condition for up to two years. Keeping in touch with you and checking on your condition helps us look at the long-term effects of the study.
ARE THERE ANY BENEFITS TO TAKING PART IN THE STUDY?	If you agree to take part in this study, the investigational study drug may help control your cancer. This may or may not make you feel better or live longer. We hope that in the future the information learned from this study will benefit other people with your condition. If proven effective, TVEC may be developed into a new therapeutic approach for treating human peritoneal surface dissemination of gastrointestinal, fallopian tube, ovarian or primary peritoneal cancers.
WHAT ARE THE MAIN RISKS OF THE STUDY?	There are risks to this study drug that are described in this document. Some risks include: flu like illness, injection site pain, joint pain, headache, arm or leg pain, and diarrhea. We will watch for side effects during study treatment and do what we can to relieve them. But you should know that side effects can be serious, even life-threatening, or may not go away. The possible

	side effects will be explained in more detail later in this form. There may be other side effects we don't know about yet. For details and a list of risks you should know about, please see the "What Are the Potential Risks and Discomforts of the Study" section below.
DO I HAVE OTHER OPTIONS BESIDES TAKING PART IN THE STUDY?	Your other choices may include the following: • Getting treatment or care for your cancer without being in a study • Depending on the therapies that you have already received, there may be other potentially beneficial approved treatments available for your cancer. These treatments may shrink tumors, delay progression of cancer, provide symptom relief, or prolong your life and could include chemotherapy (for example, platinum-based chemotherapy) or drugs that target a specific abnormality in some cancers. You should discuss these options with your doctor. • Taking part in another study. • Getting no treatment • Getting comfort care (also called palliative care) only. This type of care helps reduce pain, tiredness, appetite problems, and other problems caused by the cancer. It does not treat the cancer directly. Talk to your doctor about your choices, including the risks and benefits of each choice, before you decide if you will take part in this study.
QUESTIONS ABOUT THE STUDY?	For questions, concerns, or complaints about the study, please contact Dr. MacLaughlan at (312) 413-9874 or email at smacdav@uic.edu. If you have a research related injury, you should immediately contact Dr. MacLaughlan at (312) 413-9874, or call (312) 996-7000 and request to speak to the medical oncology fellow on call, or dial 911. If you have questions about your rights as a study subject; including questions, concerns, complaints, or if you feel you have not been treated according to the description in this form; or to offer input you may call the UIC Office for the Protection of Research Subjects (OPRS) at 312-996-1711 or 1-866-789-6215 (toll-free) or e-mail OPRS at uicirb@uic.edu.

	If you have questions or concerns regarding your privacy rights under HIPAA, you should contact the University of Illinois HIPAA Privacy Office at (844) 341-2201 or hipaa@uillinois.edu.

Please review the rest of this document for details about these topics and additional things you should know before making a decision about whether to participate in this research. Please also feel free to ask the study team questions at any time.

Who may participate in the study?

You are being asked to participate in the research study because you have stage IV peritoneal surface dissemination of gastrointestinal, fallopian tube, ovarian, or primary peritoneal cancer (peritoneal carcinomatosis). Research studies are voluntary and include only people who choose to take part. Please read this consent form carefully and take your time making your decision. As your study doctor or study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. We encourage you to talk with your family and friends before you decide to take part in this research study. The nature of the study, risks, inconveniences, discomforts, and other important information about the study are listed below.

The purpose of this study is to find out what effects, good and/or bad, Talimogene Laherparepvec (TVEC) has on you and your cancer.

TVEC is a drug that will be given in your abdomen that is an oncolytic virus. This means that it is a genetically modified version of the herpes virus that is designed to reproduce in tumor tissue and stimulate your immune system to attack the tumor cells. TVEC is FDA approved for treatment of individual lesions in patients with metastatic melanoma, but is considered investigational in peritoneal carcinomatosis. The word "investigational" means that the study drug is being tested in research studies and is not approved by the U.S. Food and Drug Administration (FDA) for this use.

Approximately 11 subjects may be involved in this study at UIC. Up to 45 patients may be involved in this research across all participating research sites. This includes 11 to 34 subjects in the Dose Escalation Cohort and 11 subjects in the Dose Expansion Cohort.

What procedures are involved?

This research will be performed at the Outpatient Care Center at the University of Illinois, located at 1818 West Taylor Street, OCC 1E.

If you agree to be in the study, you will be asked to do the following procedures:

Screening:

If you agree to be in this study, you will be asked to sign and date this consent form. You will have the following tests and procedures to make sure that you are eligible to participate and to ensure that the study drug does not pose a special risk to you:

- Physical exam and medical history
- Demographics (information such as your gender, race, age, etc.)

- List of medications that you are taking
- Vital signs (temperature, blood pressure, heart rate, and weight)
- CT scans or MRI scans for tumor measurement
- Blood tests will be taken for the following:
    - Routine blood tests – these tests will evaluate blood cell counts, blood chemistry, liver and kidney function, and how well your blood clots.
    - Blood tumor markers – this test can indicate whether your tumor is responding to the study drug.
    - Pharmacogenomics – this test will help indicate how your genes affect your response to the study drug.
    - If you are a woman able to bear children, you will also have a small blood sample taken for a pregnancy test. Pregnant women are not eligible to participate in this study.

Peritoneal Catheter Placement

After you are determined to meet eligibility for this study, you will have a catheter placed within 2 to 6 days prior to starting treatment. This catheter is a small flexible tube that will be inserted into the wall of your abdomen to allow the study drug to be put in.

Study Drugs

If the exams, tests, and procedures show that you can be in the study, and you choose to take part, you will be enrolled in the study.

On the first day of the study drug infusion, the planned dose of TVEC will be delivered via the peritoneal catheter in 500 mL of normal saline. After the infusion, you will roll onto your right side, wait 10 minutes, then roll to the left side and wait an additional 10 minutes, and repeat this procedure of rolling to the right side and the left side every 10-15 minutes for one hour. Then, you will be observed for an additional hour to make sure you tolerated the study drug infusion well.

You will have study drug infusion as described above on Day 1 and 21 of the first 5-week cycle. Each subsequent cycle will be 2 weeks long, and study drug will be administered on day 1 of each cycle. Study drug infusion will end after the completion of cycle 4.

For your safety, you will be monitored to be sure any side effects are prevented or minimized. This will require regular clinic visits, blood and urine tests, and radiology tests. These tests to check you and your cancer are part of your routine care. You will continue to receive study drug until the end of cycle 4, or if you experience excessive side effects or choose to withdraw from the study.

Assessments During Drug Regimen:

Day 1 of Cycle 1

- Physical examination
- Vital signs (every 10-15 minutes for one hour, then again after an additional hour of observation)

- List of your medications
- Routine blood tests, including blood cell count and blood chemistry (prior to study drug infusion)
- Urine pregnancy test prior to study drug infusion (only for women of childbearing potential)
- Viral load – blood and urine tests that measure the amount of the TVEC virus present in your body (done prior to study drug infusion)
- Viral antibody titers – blood test used to help measure how many antibodies your body is producing in response to TVEC (prior to study drug infusion)
- Peritoneal cytokines – some fluid from your peritoneal catheter will be used to help measure how your immune system is responding to the study treatment (prior to study drug infusion)
- Plasma for protein multiplex arrays – blood test to measure how your immune system is responding to the study treatment (prior to study drug infusion)
- Immune cells – blood and some fluid from your peritoneal catheter will be collected to help measure how your immune system is responding to the study drug (prior to study drug infusion)
- TVEC administration

Day 21 of Cycle 1

- Physical examination
- Vital signs (every 10-15 minutes for one hour, then again after an additional hour of observation)
- List of your medications
- Routine blood tests, including blood cell count and blood chemistry (prior to study drug infusion)
- Urine pregnancy test prior to study drug infusion (only for women of childbearing potential)
- Viral load (prior to study drug infusion)
- Viral antibody titers (prior to study drug infusion)
- Peritoneal cytokines (prior to study drug infusion)
- Plasma for protein multiplex arrays (prior to study drug infusion)
- TVEC administration

Days 8, 15, and 28 of Cycle 1

- Physical examination
- Vital signs
- List of your medications
- Routine blood tests, including blood cell count and blood chemistry
- Viral load

Day 1 of Cycles 2, 3, and 4

- Physical examination

- Vital signs (every 10-15 minutes for one hour, then again after an additional hour of observation)
- Routine blood tests, including blood cell count and blood chemistry
- Urine pregnancy test prior to study drug infusion (only for women of childbearing potential)
- Viral load (prior to study drug infusion)
- Plasma for protein multiplex arrays (prior to study drug infusion)
- TVEC administration

Day 1 of Cycles 2 and 4
- Immune cells (prior to study drug infusion)
- Peritoneal cytokines (prior to study drug infusion)

Day 14 of Cycle 4
- CT scans or MRI scans for tumor measurement
- Blood tumor markers

30 Days (+/-7 Days) After Final Dose
- Physical examination
- Vital signs
- Routine blood tests, including blood cell count and blood chemistry
- Pregnancy test (women of childbearing potential only)
- Viral load
- Peritoneal cytokines
- Plasma for protein multiplex arrays
- Study nurse will follow up with you every 12 weeks until your disease progresses or you start new anti-cancer therapy
- Tumor tissue – archived tumor from your primary diagnosis will be collected at the end of the study

Does the study involve genetic testing?

The cells of your body contain deoxyribonucleic acid or DNA for short. DNA is passed down from your parents. It carries the genes that determine physical features such as the color of your hair and eyes. Differences in our genes help explain why we all look different. They may also determine how different people get certain diseases and respond to drug treatments. The use of genetic material in research to study the causes of disease and to help understand how individuals respond to drug treatments is called genetic research.

Genomic information relates to the structure and function of all of the genetic material in your body.

We will submit your genomic information to a repository to be used for scientific purposes. A repository contains information from many people. Some repositories are maintained by the

University of Illinois at Chicago (UIC), some are maintained by the federal government, and some are maintained by private companies or other academic institutions. Other researchers can take information from the repository and use it in their studies. Their studies may be similar to this one or may be completely different.

We will label your genomic information with a code, instead of your name or other information that people could use to directly identify you. Even so, there is a possibility that when your genomic information is combined with other information available to researchers, either now or in the future, they may be able to identify a group you belong to (like an ethnic group or a disease population) or, less likely, you personally.

The genetic studies described are for research purposes only. Therefore, you will receive no results from this study (except as described above and in this section). It is not the purpose of this study to look for or provide you with any medical information or diagnoses relating to your present condition or any other disease or illness. The research tests are not being used as diagnostic tests for any disease or illness. Your participation in this study is not a substitute for your regular medical care or check-ups.

Through this research, we may find that you have an abnormal gene or gene product (RNA or protein) which indicates a risk for developing a disease at some time in the future. It is also possible that the research results may indirectly provide unexpected personal information about you or your family (such as ethnic/racial background or an unknown genetic relationship between family members). Please talk with the study doctor if you have any questions or concerns about the genetic testing being done in this research study. He/she may also refer you to a genetic counselor for further information.

It is possible that this study will identify information about you that was previously unknown, such as disease status or risk. There are no plans to provide this information to you or your physician.

Optional Consent for use of Leftover Samples for Future Biomarker Research

With your permission, your blood and/or tissue samples may be shared anonymously with other investigators for research purposes. The samples may be used for study of disorders unrelated to the one(s) in your family. Such research will be strictly anonymous, in that no identifying information that would link the samples to you is provided to the researcher. An ethics board will review any such research prior to access being given to your samples. This secondary use will in no way compromise the study of the disorder(s) in your family or the use of your samples as part of this study.

Tissue, blood, or other samples collected as part of this study may be valuable for scientific, research, or teaching purposes or for the development of a new medical or commercial product. DUHS and/or the developers will assert all rights of ownership in the samples and all rights arising from use of the samples. There is no plan to compensate you for any use of the samples.

Please indicate below whether or not you wish to provide your consent to take part in this optional research.

I agree to provide an additional blood sample for the research described above.

☐ Yes ☐ No Please initial here: _____ Date: _____

What will happen with my information and/or biospecimens used in this study?
Biospecimens are samples of material, such as urine, blood, tissue, cells, etc. Biospecimens are stored in a repository or bank and are used for laboratory research. We may use biospecimens collected as a part of this study for whole genome sequencing, which describes the positions of genes (the basic unit of heredity).

Your identifiable private information and/or identifiable biospecimens collected for this research study may be used for future research studies and/or shared with other researchers for future research. If this happens, information which could identify you will be removed before any information and/or biospecimens are shared. Once the identifying information is removed, the information and samples cannot be withdrawn from further use. You will not be asked for additional consent.

Will I receive my results from the study?
We will not share results of the study with you.

What are the potential risks and discomforts of the study?
Drugs used for anti-cancer therapy often have some undesirable side effects. It is important to be aware that there may be other side effects that are not yet known and cannot be foreseen. Side effects may go away after the study drug has stopped, but it is also possible that side effects may last a long time or forever. They may range from mild to life threatening or even lethal. It is possible that side effects can be minimized with additional treatments. Many side effects can be prevented or minimized by noticing the side effects early while they are still mild. Therefore, it is important to tell the study doctor or study nurse immediately about any changes in health that may have occurred even if you do not think they are related to the study. Your study doctor may give you treatment to help control side effects. If your study nurse or study doctor explains how to apply some preventative measures (for example to reduce risk of skin toxicity) please listen carefully. As a result of your participation in this study, you are at risk for the following side effects. You should discuss these with the study doctor and your regular health care provider if you choose.

As of 26 October 2020, more than 6,055 patients have received talimogene laherparepvec with approximately 1,416 patients having received talimogene laherparepvec in research studies and approximately 4,639 people were prescribed talimogene laherparepvec (IMLYGIC®) after it was approved for sale.

Side effects that other people have had in research studies that are thought to have been caused by talimogene laherparepvec are:

Very Common Side Effects ***(may affect more than 1 person in 10)***

- Flu like illness: chills, fever, feeling tired, muscle pain, nausea and vomiting

- Injection site pain
- Headache
- Joint pain
- Arm or leg pain
- Diarrhea
- Constipation

Common Side Effects ***(may affect between 1 and 10 people in every 100)***

- Injection site reactions: bleeding, redness, swelling, inflammation
- Skin infection caused by bacteria at the site of injection: symptoms may include fever, chills, redness or swelling at the injection site or the site of the tumor, and may require hospitalization for antibiotic treatment
- Wound complication at the injection site (secretion or discharge)
- Pain: pain after procedure, in the tumor, in the abdomen, throat pain, pain in the armpit or groin
- Abdominal discomfort
- Cold sore or fever blister in mouth (Oral herpes)
- Low red blood cell count (Anemia)
- Not feeling well (Malaise)
- Weight loss
- Dehydration
- Bruise
- Dizziness
- Skin or face becomes warm and reddened (Flushing)
- Rash
- Inflamed skin (Dermatitis)
- Blood clot (Deep vein thrombosis)
- Autoimmune Reactions: (a reaction of your body's immune system fighting your body's own tissues) have been reported in some patients administered talimogene laherparepvec. Examples of autoimmune reactions that have been reported in patients receiving talimogene laherparepvec include:
    - Inflammation of the kidneys (glomerulonephritis)
    - Inflammation of the blood vessels (vasculitis)
    - Inflammation of the lungs (pneumonitis)
    - Areas of skin with loss of color (vitiligo)
    - If you already have psoriasis (itchy, flaky patches or scaling of the skin), it may get worse

  It is possible that an autoimmune reaction could occur in any part of the body. Please tell your doctor if you have had any type of autoimmune disease before

administration of talimogene laherparepvec, and all treatments you are receiving for the disease.

Uncommon Side Effects ***(which may affect between 1 and 10 people in every 1000)***

- Injection site reactions: warmth, incision site infection
- Eye infection caused by herpes virus (Herpetic keratitis)
- Difficulty breathing: People receiving talimogene laherparepvec have experienced difficulty breathing or the sensation of shortness of breath. In addition, if you have a tumor in your neck, your doctor may warn you that you might experience compression of your airways during treatment with talimogene laherparepvec. This might require a surgical procedure on the neck to open a direct airway. This occurred in a talimogene laherparepvectreated patient who had a similar problem before treatment. A tube might need to be inserted into the opening in your throat. This tube may be connected to a machine to help you breathe.
- Plasmacytoma (a collection of abnormal antibody-producing white blood cells) in the area where talimogene laherparepvec is injected. Plasmacytoma may be associated with multiple myeloma (a cancer of white blood cells affecting the bone marrow).
- Symptoms of delayed wound healing at or around the injection site such as injection site discharge, foul odor, or dead tissue at the injection site. If you notice symptoms of delayed wound healing at the injection site(s), especially if you have risk factors such as diabetes, poor blood circulation, have had radiation to the site, you should contact the study doctor or his/her study staff immediately.

Injection Site Reactions – Reactions at or near the area of the injection have been seen in other people administered talimogene laherparepvec. Symptoms include bleeding, redness, swelling and inflammation of the injection site. Skin infection caused by bacteria at the site of injection which may require hospitalization for antibiotic treatment have also been reported. Other symptoms may include warmth at the injection site or symptoms of delayed wound healing at or around the injection site such as injection site discharge, foul odor, or dead tissue at the injection site. If you notice symptoms of delayed wound healing at the injection site(s), you should contact the study doctor or his/her staff immediately.

Side Effects with Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF) – Talimogene laherparepvec contains genetic material that makes human GM-CSF. Human GM-CSF is a medicine used to treat patients with blood cell counts that are all low. Known side effects of human GM-CSF include, but are not limited to, musculoskeletal pain, fever, chills, shortness of breath, rash, fatigue, gastrointestinal effects, and fluid around heart and lungs. Although the amount of human GM-CSF released when treating tumor lesions with talimogene laherparepvec is very small, these side effects may still occur and your doctor will be looking for them.

Transmission of Talimogene Laherparepvec – You should always observe proper hygiene (wash your hands with warm water and soap after touching your injected site or handling the dressings) to avoid potentially spreading talimogene laberparepvec to other persons.

There have not been reported cases of spreading of talimogene laherparepvec to close contacts or family members in clinical trials to date. However TVEC could potentially be spread to your family members or other close contacts (household members, care-givers, sex partners, or someone you share a bed with) at any time after your tumor(s) are injected with the study drug. This may occur if your family member or other close contact touches the injection site or has contact with your body fluids or with the inside of the dressing(s) covering your injection site(s).

Spreading TVEC may be more likely if your close contact has a break in the skin or mucous membranes that comes into contact with your injection site or your body fluids. In patients treated with TVEC in clinical trials, TVEC has been found on the surface of the injected tumors, and on the outside of the dressings that covered these injection sites. All close contracts should wear gloves when handling materials that have come in contact with the injection catheter for a minimum of two weeks following each administration.

Talimogene laherparepvec have also been detected in patients' blood and urine, and in the patient's mucous membranes of the mouth and genitals, no samples had detectable talimogene laherparepvec 30 days after the end of treatment. For patients who had talimogene laherparepvec presence in the surface of injected tumors, no samples had detectable talimogene laherparepvec 60 days after end of treatment.

If a close contact has been exposed to TVEC, it is possible that they could develop symptoms similar to that of a herpes virus infection (see below). However, the chance of this happening is low due to the changes in TVEC that make it different from the naturally occurring herpes simplex virus, but you should know how to recognize these symptoms. Please contact the study doctor or study staff if a close contact develops herpes virus infection symptoms.

Most adults in the population have been exposed to the naturally occurring herpes simplex (also known as "cold sore") virus (HSV-1). Common signs and symptoms of the naturally occurring herpes simplex virus include:

- Sores around the mouth ("cold sore", "fever blister") or the genitals ("genital sore").
- Blisters may develop on the fingers, ears, or face.
- Eye infection (herpetic keratitis) with eye pain, light sensitivity, discharge from the eyes or blurry vision.
- Abdominal pain and infections, and inflammation inside the abdomen (infrequently).
- Rarely, serious infections of the brain (encephalitis) or spinal cord, causing paralysis (unable to move) have been reported. Signs may include fever, confusion or other behavior changes, headache, numbness and pain in the legs, constipation, or difficulty with urination.
- Life-threatening infections (disseminated herpes) can develop in people with a weakened immune system.
- Whenever possible contact with immunosuppressed persons should be avoided to minimize risk of transmission.

After infection, the naturally occurring herpes virus may travel to spinal nerve roots. The virus can reactivate from the nerve roots and cause recurrent cold sores or other signs of infection as

described above. Stress, other illness, or menstruation are common triggers for reactivation of the naturally occurring virus.

Signs and symptoms of infection with TVEC could be similar to those described above, although TVEC has been changed to reduce the chance of this happening.

In the event a close contact becomes infected with herpes virus, it is recommended that they be treated with two days of intravenous acyclovir (5 mg/kg every 8 h) followed by eight days of oral valacyclovir (1000 mg twice daily). Talk to your doctor if you have any questions and take the necessary precautions to reduce the chances of transmission to close contacts.

Delay in Response with TVEC Administration – Given that TVEC may help by stimulating your immune system (immunotherapy), it is possible that there can be a delay in your body responding to the study drug. In addition, you may also see an increase in the size of existing tumors and/or the development of new tumors before potentially seeing a response to TVEC.

Allergic Reactions – As with any medication, you may have an allergic reaction to TVEC. Symptoms of an allergic reaction in general may include headache, rash, itching, flushing, swelling, shortness of breath, nausea and sometimes vomiting. Severe allergic reactions can cause dizziness, severe skin reactions, difficulty breathing or swallowing, a decrease in blood pressure, and could be life threatening. If you have symptoms of an allergic reaction, you should contact the study doctor or his/her study staff immediately. If you have had an allergic reaction to TVEC or any of its ingredients, you should inform your doctor.

Risk of Peritoneal Catheter:

There are several risks associated with the use of a peritoneal catheter.

The risk of **bowel perforation** is less than 1%, and it usually occurs during entry into the abdominal cavity or when the catheter and stylet (probe) are moved further into the abdomen. Surgical exploration is necessary with repair of the perforation and removal of the catheter.

Bleeding is rarely a significant problem after peritoneal catheter placement. This typically does not require medical intervention outside of holding pressure at the exit site.

Wound infection is uncommon and often can be treated with antibiotics when it is on the surface. If the wound is deeper, then it may need to be drained surgically.

Outflow failure may be due to several causes including clots or fibrin (protein) in the catheter, a kink in the tunnel under the skin, placement of the catheter in the omentum (organ above the intestines), blockage from omentum, or adhesions (scar-like tissues). A number of treatments might be required including flushing with a clot dissolving agent and repositioning of the catheter.

Leakage of the infusion solution may be identified by the presence of drainage at the exit site or the appearance of a bulge underneath the catheter site. An x-ray study of the catheter will determine the method of treatment that is pursued.

Risk of Peritoneal Catheter – TVEC Administration:
In this study, TVEC will be administered into the peritoneum via intraperitoneal catheter. Since this administration method is different than the approved method of administering the drug normally, there may be additional associated risks. These include:

- Ileus (the inability of the intestine (bowel) to contract normally and move waste out of the body)
- Bowel perforation (rupture) due to tumor response
- Peritonitis (inflammation of the membrane lining the abdominal wall and covering the abdominal organs)

Risks of Drawing Blood:
Risks associated with drawing blood from your arm include momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or fainting are also possible, although unlikely.

Risk of CT Scan:
Computed Tomography (CT) is a way to make x-ray images of the inside of the body. The CT scanner is a doughnut-shaped machine that uses x-rays to create computer pictures that show structures inside your body more clearly than regular x-ray pictures. During the procedure, a technologist will take you into the CT scan room where you will lie down on the subject table (usually on your back) inside of the CT machine. You should get comfortable because it is very important that you not move during certain parts of the test.

CT examinations differ depending on the part of your body being studied. For example, if your abdomen is being studied, a series of pictures will be taken from your lower chest to your lower pelvis. During the study, you will be asked to hold your breath so that the pictures will not be blurred. The machine will make some noise, and the table will move during the scan. Also, you may receive signals from the technologist or from the machine about your breathing. Before or during the study, you may be given an injection of contrast liquid in your vein to allow the radiologist to obtain clearer images of your organs. If you have any discomfort during the test or after the injection, be sure to tell the technologist.

Risk of MRI Scan:
Magnetic resonance imaging (MRI) uses a magnet and radio waves to make diagnostic medical images of the body. There have been no ill effects reported from exposure to the magnetism or radio waves used in this test. However, it is possible that harmful effects could be recognized in the future. A known risk is that the magnet could attract certain kinds of metal. Therefore, we will carefully ask you about metal within your body (this includes certain dyes found in tattoos). If there is any question about potentially hazardous metal within your body, you will not be able to have an MRI.

If you have an MRI as part of your tumor assessment, you will enter a large room in which a magnet is present. You will be placed on a narrow bed and then slide into a small tunnel approximately 6 feet in length and 25 inches in diameter. You will be asked to lie still for about one hour on this bed. You will hear a loud machine-like noise. You may be asked to have a

harmless monitoring device applied during the study. During the study, you can have voice contact and physical contact with someone in attendance if you desire.

Risks of Radiation:
You will have a number of CT scans or MRI scans that are part of the regular care for your condition, and you would have them whether or not you participate in this research. These studies will not add to the risk due to participating in the research. However, if you have concerns about the overall radiation exposure or MRI safety issue, you should discuss them with your physician.

Sometimes subjects have allergic reactions to the dyes used in imaging scans. This is rare. It can involve itching or rash. In severe cases, you may have difficulty breathing and dangerous lowering of your blood pressure. If you know that you have an allergy to the dye, or to iodine or shellfish, please let your study doctor and radiologist know.

Drug and Food Interactions:
For your safety, you must tell the study doctor or nurse about all the prescribed medical foods and drugs, herbal products, over-the-counter (OTC) drugs, vitamins, natural remedies, and alcohol that you are taking before you start the study and before starting to take any of these products while you are on the study.

There may be risks from the study that are not known at this time. In addition, the risks for participation in this study may be different than what has previously been determined.

A risk of this research is a loss of privacy (revealing to others that you are taking part in this study) or confidentiality (revealing information about you to others to whom you have not given permission to see this information).

While we believe that the risks to you and your family are very low, we are not able to know all of the risks from taking part in genetic research studies. Your privacy will be protected to the fullest extent possible. Certain health concerns that affect you and your blood relatives might be found as inherited traits are studied. Even though your genes are unique, you share some of the same genes with your blood relatives. In addition, there may be undue stress, anxiety, or embarrassment resulting from inadvertent disclosure of information on family relationships, ethnic heritage, or potentially stigmatizing conditions.

There is a Federal law called the Genetic Information Nondiscrimination Act (GINA). In general, this law makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. For example, life insurance companies may charge a higher rate based on this information. GINA also does not protect you against discrimination if you have already been diagnosed with the genetic disease that is being tested in this research study.

What are the potential reproductive risks of the study?

For women: The effects of the study drug on a developing pregnancy are not well understood, although herpes viruses are known to cause complications during pregnancy. Women who are pregnant or breastfeeding are excluded from this study.

If you are a woman who could possibly become pregnant (you have not completed menopause, or you have not had a hysterectomy and/or both tubes and/or both ovaries removed), and you have a partner who is able to father children, a blood pregnancy test will be done (using 1 teaspoon of blood drawn from a vein by needle-stick), and it must be negative before you can continue in this study. In women 40 years old and older, blood pregnancy tests can sometimes give a false positive or indeterminate result, and additional testing may be required.

You and your partner must agree to either abstain completely from vaginal intercourse for the duration of this study and for 90 days after the last dose of study drug, or agree to use highly effective methods of contraception for the same length of time. Highly effective methods include (a) partner vasectomy, (b) bilateral tubal ligation, (c) intrauterine devices (IUDs), (d) hormonal implants (e.g., Implanon), (e) other hormonal methods (birth control pills, injections, patches, vaginal rings) plus a barrier method (condoms, diaphragms, cervical caps) plus spermicide, or (f) condoms plus a diaphragm or cervical cap plus spermicide. If you are not currently using one of these methods, your study doctor will discuss options with you, given your medical condition, your personal preferences, and the level of protection required by this study. Because no birth control method is 100% effective, you should contact your study doctor immediately if you think there is any chance you could be pregnant.

For men: The effects of the study drug on a developing pregnancy that began while the father was taking the drug are unknown, and the study drug may be present in semen and transmitted to a partner during sexual activity. If you have a partner who could possibly become pregnant (she has not completed menopause, or she has not had a hysterectomy and/or both tubes and/or both ovaries removed), you must agree to either abstain completely from vaginal intercourse for the duration of the study and for 90 days after the last dose of study drug, or use a condom every time you have intercourse for the same length of time. This is true even if you have had a vasectomy (since vasectomy does not prevent transmission in semen). If your partner is currently pregnant or breastfeeding, you must use a condom for all types of intercourse. You should inform your partner about the potential risks of the study drug. If she is not currently using another method of contraception, she should consider discussing options with her health care provider. If she does become pregnant during your participation in the study, you will need to report it to the study doctor, and she should promptly notify her doctor.

What about privacy and confidentiality?

Efforts will be made to keep your personal information confidential; however, we cannot guarantee absolute confidentiality. In general, information about you, or provided by you, during the research study, will not be disclosed to others without your written permission. However, laws and university rules might require us to tell certain people about you. For example, study information which identifies you and the consent form signed by you may be looked at and/or copied for quality assurance and data analysis include:

- Representatives of the university committee and office that reviews and approves research studies, the Institutional Review Board (IRB) and Office for the Protection of Research Subjects.
- Other representatives of the State and University responsible for ethical, regulatory, or financial oversight of research.
- Government Regulatory Agencies, such as the Office for Human Research Protections (OHRP).
- The sponsor of the research study, Dan Blazer III, MD at Duke University Medical Center, and funder, Amgen.
- Authorized Representatives of the sponsor.
- The Food and Drug Administration
- The manufacturer of the drug, device or biologic, Amgen.
- UIC Office for the Protection of Research Subjects, State of Illinois Auditors

A possible risk of the study is that your participation in the study or information about you and your health might become known to individuals outside the study. Your research data will be coded to prevent access by unauthorized personnel. Your study information will be given to the sponsor with your information in a coded format.

Your individual data will be stripped of all direct and indirect identifiers after the analysis of the data.

When the results of the study are published or discussed in conferences, no one will know that you were in the study.

A description of this study 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.

Will health information about you be created, used or shared with others during this study?

State and federal laws, including the Health Insurance Portability and Accountability Act (HIPAA), require researchers to protect your health information. This section of this form describes how researchers, with your authorization (permission), may use and release (disclose or share) your protected health information in this research study. By signing this form you are authorizing Dr. MacLaughlan and her research staff to create, get, use, store, and share protected health information that identifies you for the purposes of this research.

The health information includes all information created and/or collected during the research as described within this consent form and/or any health information in your medical record that is needed for the research and that specifically includes:

- Demographic information, such as your name, date of birth, gender, address including zip code, telephone number, race, and ethnicity;
- Your cancer history and diagnosis;

- Specific information about any cancer treatments received, including previous treatment(s) you may have had;
- Information about other medical conditions that may affect your treatment;
- Medical data, including your laboratory test results, results of histological review of tissue biopsies, CT scans, and MRI scans;
- Information about side effects (adverse events) that you may experience, and how these were treated;
- Long-term information about your general health status and the status of your disease;
- Numbers or codes that identify your records, such as medical record number.

The researchers may need to use health information from your doctors not at UIC. In this case, you will be asked to sign a separate authorization (medical release) form requesting your non-UIC doctor to give the information to Dr. MacLaughlan.

During the conduct of the research, the researchers may use or share your health information:
- With each other and with other researchers involved with the study;
- With law enforcement or other agencies, when required by law;
- With the sponsor/funding agency of the research, Amgen, as required to conduct the research and if the research results need to be confirmed;
- With non-UIC collaborators of the research study: Duke University Medical Center
- With representatives of government agencies (i.e., Food and Drug Administration), review boards including the University of Illinois at Chicago Institutional Review Board, the University of Illinois Medical Center and its representatives, and other persons who watch over the safety, effectiveness, and conduct of research; and
- U.S. government agencies that are responsible for overseeing public health concerns such as the Centers for Disease Control (CDC) and federal, state, and local health departments.

If all information that identifies you is removed from your health information, the remaining information is no longer subject to the limits of this Authorization or to the HIPAA privacy laws. Therefore, the de-identified information may be used and released by the researchers (as permitted by law) for other purposes, such as other research projects.

You will not have access to the health information related to this research study until the study is done. However, this information is available to your doctor in the case of an emergency. At the end of the study, you will again have access to health information that is normally within your medical records (treatment, insurance and billing information). However, the researcher may not give you access to the research records or information that is not usually kept in your medical record, as it is not required by HIPAA.

How will your health information be protected?

The researchers, Amgen, and Duke University Medical Center agree to protect your health information and will only share this information as described within this research consent/authorization form.

When your health information is given to people outside of the research study, those agencies that receive your health information may not be required by federal privacy laws (such as the

Privacy Rule) to protect it. They may also share your information with others without your permission, if permitted by laws that they have to follow.

What if I am injured as a result of my participation?

If you get ill or injured from being in the study, UIC will help you get medical treatment. You should let the study doctor know right away that you are ill or injured. If you believe you have become ill or injured from this study, you should contact Dr. MacLaughlan at (312) 413-9874. In the event of an emergency, call (312) 996-7000 and request to speak to the medical oncology fellow on call, or dial 911.

You should let any health care provider who treats you know that you are in a research study. If you do seek medical treatment, please take a copy of this document with you because it may help the doctors where you seek treatment to treat you. It will also provide the doctors where you seek treatment with information they may need if they want to contact the research doctors.

You or your health insurance plan will be billed. No money has been set aside to pay the costs of this treatment. Health insurance plans may or may not cover costs of research-related injury or illness. You should check with your insurance company before deciding to participate in this research study. Costs not covered by insurance could be substantial.

UIC has not set aside any money to pay you or to pay for your treatment if you get ill or injured from being in the study. There are no plans for the University or the study supporter, Amgen, Inc., to provide other forms of compensation (such as lost wages or pain and suffering) to you for research related illnesses or injuries. The only exception to this policy is if it is proven that your injury or illness is directly caused by the negligence of UIC.

By signing this form, you are not giving up any legal rights to seek compensation of injury.

What are the costs for participating in this research study?

If you take part in this study, you may have to pay extra costs.

You or your insurer will be responsible for paying for the cost of the following: any standard medical care that you receive under this study.

The study sponsor Amgen has agreed to pay for services and procedures that are done solely for research purposes. Please talk with the PI/study team about the specific services and procedures that the sponsor will pay for, and the ones for which you or your insurance will be responsible.

If you have health insurance the insurance may or may not pay for your participation in the research. You will have to pay for any co-payments, deductibles or co-insurance amounts that your insurance coverage requires.

If you do not have insurance, you will be billed for the amount you have to pay.

Will I be reimbursed for any of my expenses or paid for my participation in this research study?

You will not be offered payment for being in this study.

What other things should I know?

Your health care provider may be a researcher on this study, and as a researcher, is interested in both your clinical welfare and in the conduct of this study. Before entering this research study or at any time during the research study, you may ask for a second opinion about your care from a health care provider who is not associated with this research study. You are not obligated to participate in any research study offered by your health care provider. Your participation in this research study is voluntary and you do not have to participate. The decision to not participate will not affect your clinical care now or in the future.

Will I be told about new information that may affect my decision to participate?

During the course of the study, you will be informed of any significant new research findings (either good or bad), such as changes in the risks or benefits resulting from participation in the research or new alternatives to participation, that might cause you to change your mind about continuing in the study. If new information is provided to you, your consent to continue participating in this study may be re-obtained.

Can I withdraw or be removed from the study?

If you decide to participate, you have the right to withdraw your consent and leave the study at any time without penalty.

For your safety, you should consider the researcher's advice about how to leave the study. If you leave the study before the final planned study visit, the researcher may ask you to complete the final steps.

Dr. MacLaughlan may ask you to return for a checkup before you stop your study drug if she thinks that stopping the drug suddenly may harm you. She may also ask you to complete the tests that would ordinarily occur when a person completes the study.

We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

The researchers and sponsor also have the right to stop your participation in this study without your consent if:

- They believe it is in your best interests;
- You were to object to any future changes that may be made in the study plan;
- If your condition gets worse, or if you have serious side effects.

The sponsor or regulatory agencies may stop this study at any time without your consent (reasons may include unanticipated drug toxicity or lack of effectiveness). If this occurs, you will be notified and your study doctor will discuss other options with you.

If you agree to allow your tissue to be kept for future research with identifying information that could link your sample to you, you are free to change your mind at any time. We ask that you contact Dr. MacLaughlan in writing and let her know you are withdrawing your permission for your identifiable tissue to be used for future research. Her mailing address is below. At that time we will ask you to indicate in writing if you want the unused identifiable tissue destroyed or if your samples (having all identifying information removed that would link the sample to you) could be used for other research.

Your samples and/or data may be stored and shared for future research without additional informed consent if identifiable private information, such as your name and medical record number, are removed. If your identifying information is removed from your samples or data, we will no longer be able to identify and destroy them.

The use of your samples may result in commercial profit. You will not be compensated for the use of your samples other than what is described in this consent form.

If you choose to no longer be in the study and you do not want any of your future health information to be used, you must inform Dr. MacLaughlan in writing at the address on the first page. Dr. MacLaughlan may still use your information that was collected prior to your written notice.

Your Authorization for release of health information for this research study does not have an expiration date, but can be canceled sooner if you decide to withdraw your permission.

You may change your mind and cancel this Authorization at any time. To cancel this Authorization, you must write to:

Shannon MacLaughlan, MD
840 S. Wood St.,
263 CSN MC 808
Chicago, IL 60612

If you cancel this Authorization, you may no longer be allowed to take part in the research study. Even if you cancel this Authorization, the researchers may still use and disclose health information they have already obtained as necessary to maintain the integrity and reliability of the research and to report any adverse (bad) effects that may have happened to you.

Remember:
Your participation in this research study is voluntary. Your decision whether or not to participate will not affect your current or future relations with the University. If you decide to participate, you are free to withdraw at any time without affecting that relationship.

Right to Refuse to Sign this Authorization
You do not have to sign this Consent/Authorization. However, because your health information is required for research participation, you cannot be in this research study if you do not sign this

form. If you decide not to sign this Consent/Authorization form, it will only mean you cannot take part in this research. Not signing this form will not affect your non-research related treatment, payment or enrollment in any health plans or your eligibility for other medical benefits.

If you have not already received a copy of the Notice of Privacy Practices, you should ask for one.

Your signature below indicates that you are providing both consent to participate in the research study and authorization for the researcher to use and share your health information for the research.

Signature of Subject or Legally Authorized Representative

I have read (or someone has read to me) the above information. I have been given an opportunity to ask questions and my questions have been answered to my satisfaction. I agree to participate in this research study. I will be given a copy of the signed and dated form.

_____	_____
Signature	Date
_____	
Printed Name	
_____	_____
Signature of Person Obtaining Consent	Date (must be same as subject's)
_____	
Printed Name of Person Obtaining Consent	
_____	_____
Signature of Parent / Guardian or Legally Authorized Representative of Subject	Date (must be same as Subject's)
_____	
Printed name of Parent / Guardian or Legally Authorized Representative of Subject	

Describe relationship to subject including the legal authority this individual has to act on behalf of the subject. (Check one below)

☐ Parent

☐ Medical Power of attorney/representative
☐ Legal guardian
☐ Health care surrogate
☐ Other; specify

_____

_____

_____

Wake Forest®
School of Medicine

Study Title: Talimogene Laherparepvec for the Treatment of Peritoneal Surface Malignancies (TEMPO)

CONCISE SUMMARY

This is a research summary to find what effects, good and/or bad, an investigational drug called Talimogene Laherparepvec (TVEC) has on you and your cancer. We hope TVEC will actively kill tumor cells and promote your own body's immune system to attack your tumor as well. If proven effective, TVEC may be developed into a new therapeutic approach for treating human peritoneal surface dissemination of gastrointestinal and ovarian cancers.

TVEC will be administered via peritoneal catheter on Day 1 and 21 of the first 5-week cycle. Each subsequent cycle will be 2 weeks long, and the study drug will be administered on day 1 of each cycle. The study drug infusions will end after the completion of cycle 4. You will have tests, exams, and procedures that are part of your standard care and for study purposes.

There are risks to this study drug that are described in this document. Some risks include: flu like illness, injection site pain, joint pain, headache, arm or leg pain, and diarrhea. There may be some unknown but potentially serious and life-threatening side effects.

If you are interested in learning more about this study, please continue reading below.

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact the Institutional Review Board at 336-716-4542 or the Research Subject Advocate at Wake Forest at 336-716-8372.

Principal Investigator: Edward Levine, MD
Department: Surgery Oncology
Phone Number: 336-713-5440 (24 hour number)

You are being asked to take part in this research study because you have stage IV peritoneal surface dissemination of gastrointestinal, fallopian tube, ovarian, or primary peritoneal cancer (peritoneal carcinomatosis). Research studies are voluntary and include only people who choose to take part. Please read this consent form carefully and take your time making your decision. As your study doctor or study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. We encourage you to talk with your family and friends before you decide to take part in this research study. The nature of the study, risks, inconveniences, discomforts, and other important information about the study are listed below.

Please tell the study doctor or study staff if you are taking part in another research study.

Edward Levine, MD will conduct the study and it is funded by Duke University. The sponsor of this study, Duke University, will pay Wake Forest Baptist Medical Center to perform this research, and these funds may reimburse part of Dr. Levine's salary.

WFU School of Medicine
Institutional Review Board
IRB Number: IRB00056815
Meeting Date Approved 12/12/2022
Version Valid Until: 9/20/2023

WHO WILL BE MY DOCTOR ON THIS STUDY?
If you decide to participate, Dr. Levine or another study physician will be your doctor for the study and will be in contact with your regular health care provider throughout the time that you are in the study and afterwards, if needed.

WHY IS THIS STUDY BEING DONE?
The purpose of this study is to find out what effects, good and/or bad, Talimogene Laherparepvec (TVEC) has on you and your cancer.

HOW DOES THIS DRUG WORK?
TVEC is a drug that will be given in your abdomen that is an oncolytic virus. This means that it is a genetically modified version of the herpes virus that is designed to reproduce in tumor tissue and stimulate your immune system to attack the tumor cells. TVEC is FDA approved for treatment of individual lesions in patients with metastatic melanoma, but is considered investigational in peritoneal carcinomatosis. The word "investigational" means that the study drug is being tested in research studies and is not approved by the U.S. Food and Drug Administration (FDA) for this use.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?
Approximately 10 people will take part in this study at Wake Forest Baptist Medical Center. Approximately 45 people will take part in this study at all sites. This includes 11 to 34 subjects in the Dose Escalation Cohort and 6 subjects in the Dose Expansion Cohort.

WHAT IS INVOLVED IN THE STUDY?
Screening:
If you agree to be in this study, you will be asked to sign and date this consent form. You will have the following tests and procedures to make sure that you are eligible to participate and to ensure that the study drug does not pose a special risk to you:

- Physical exam and medical history
- Demographics (information such as your gender, race, age, etc)
- List of medications that you are taking
- Vital signs (temperature, blood pressure, heart rate, and weight)
- CT scans or MRI scans for tumor measurement
- Blood tests will be taken for the following:
    - Routine blood tests – these tests will evaluate blood cell counts, blood chemistry, liver and kidney function, and how well your blood clots.
    - Blood tumor markers – this test can indicate whether your tumor is responding to the study drug.
    - Pharmacogenomics – this test will help indicate how your genes affect your response to the study drug.
    - If you are a woman able to bear children, you will also have a small blood sample taken for a pregnancy test. Pregnant women are not eligible to participate in this study.

Peritoneal Catheter Placement

- After you are determined to meet eligibility for this study, you will have a catheter placed within 2 to 6 days prior to starting treatment. This catheter is a small flexible tube that will be inserted into the wall of your abdomen to allow the study drug to be put in.

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Study Drugs

If the exams, tests, and procedures show that you can be in the study, and you choose to take part, you will be enrolled in the study.

On the first day of the study drug infusion, the planned dose of TVEC will be delivered via the peritoneal catheter in 500 mL of normal saline. After the infusion, you will roll onto your right side, wait 10 minutes, then roll to the left side and wait an additional 10 minutes, and repeat this procedure of rolling to the right side and the left side every 10-15 minutes for one hour. You will be observed for an additional hour to make sure you tolerated the study drug infusion well. Observation will take place in a surgical oncology room on the 4th floor of the Comprehensive Cancer Center.

You will have study drug infusion as described above on Day 1 and 21 of the first 5-week cycle. Day 1 is the first day of treatment with the study drug; 21 days later (day 21), you will receive another infusion. You will rest for 2 additional weeks without treatment to complete a cycle. Each subsequent cycle will be 2 weeks long, and study drug will be administered on day 1 of each cycle. Study drug infusion will end after the completion of cycle 4.

For your safety, you will be monitored to be sure any side effects are prevented or minimized. This will require regular clinic visits, blood and urine tests, and radiology tests. These tests to check you and your cancer are part of your routine care. You will continue to receive study drug until the end of cycle 4, or if you experience excessive side effects or choose to withdraw from the study. The maximum of blood drawn during this study will be 300 mL, or 60 teaspoons.

Assessments During Drug Regimen:

Day 1 of Cycle 1

- Physical examination
- Vital signs (every 10-15 minutes for one hour, then again after an additional hour of observation)
- List of your medications
- Routine blood tests, including blood cell count and blood chemistry (prior to study drug infusion)
- Urine pregnancy test prior to study drug infusion (Only for women of childbearing potential)
- Viral load – blood and urine tests that measure the amount of the TVEC virus present in your body (done prior to study drug infusion)
- Viral antibody titers – blood test used to help measure how many antibodies your body is producing in response to TVEC (prior to study drug infusion)
- Peritoneal cytokines – some fluid from your peritoneal catheter will be used to help measure how your immune system is responding to the study drug (prior to study drug infusion)
- Plasma for protein multiplex arrays – blood test to measure how your immune system is responding to the study drug (prior to study drug infusion)
- Immune cells – blood and some fluid from your peritoneal catheter will be collected to help measure how your immune system is responding to the study drug (prior to study drug infusion)
- TVEC administration

Day 21 of Cycle 1

- Physical examination

- Vital signs (every 10-15 minutes for one hour, then again after an additional hour of observation)
- List of your medications
- Routine blood tests, including blood cell count and blood chemistry (prior to study drug infusion)
- Urine pregnancy test prior to study drug infusion (Only for women of childbearing potential)
- Viral load (prior to study drug infusion)
- Viral antibody titers (prior to study drug infusion)
- Peritoneal cytokines (prior to study drug infusion)
- Plasma for protein multiplex arrays (prior to study drug infusion)
- TVEC administration

Days 8, 15, and 28 of Cycle 1

- Physical examination
- Vital signs
- List of your medications
- Routine blood tests, including blood cell count and blood chemistry
- Viral load

Day 1 of Cycles 2, 3, and 4

- Physical examination
- Vital signs (every 10-15 minutes for one hour, then again after an additional hour of observation)
- Routine blood tests, including blood cell count and blood chemistry
- Urine pregnancy test prior to study drug infusion (Only for women of childbearing potential)
- Viral load (prior to study drug infusion)
- Peritoneal cytokines (prior to study drug infusion)
- Plasma for protein multiplex arrays (prior to study drug infusion)
- TVEC administration

Day 1 of Cycles 2 and 4

- Immune cells (prior to study drug infusion)

Day 14 of Cycle 4

- CT scans or MRI scans for tumor measurement
- Blood tumor markers

30 Days (+/-7 Days) After Final Dose

- Physical examination
- Vital signs
- Routine blood tests, including blood cell count and blood chemistry
- Pregnancy test (women of childbearing potential only)
- Viral load
- Peritoneal cytokines
- Plasma for protein multiplex arrays

- Study nurse will follow up with you every 12 weeks until your disease progresses or you start new anti-cancer therapy
- Tumor tissue – archived tumor from your primary diagnosis will be collected at the end of the study

Optional Consent for use of Leftover Samples for Future Biomarker Research

With your permission, your blood and/or tissue samples may be shared anonymously with other investigators for research purposes. The samples may be used for study of disorders unrelated to the one(s) in your family. Such research will be strictly anonymous, in that no identifying information that would link the samples to you is provided to the researcher. An ethics board will review any such research prior to access being given to your samples. This secondary use will in no way compromise the study of the disorder(s) in your family or the use of your samples as part of this study.

Tissue, blood, or other samples collected as part of this study may be valuable for scientific, research, or teaching purposes or for the development of a new medical or commercial product. DUHS and/or the developers will assert all rights of ownership in the samples and all rights arising from use of the samples. There is no plan to compensate you for any use of the samples.

Please indicate below whether or not you wish to provide your consent to take part in this optional research.

I agree to provide an additional blood sample for the research described above.

☐ Yes ☐ No Please initial here: _____ Date: _____

We can send copies of your test results to your personal physician. Even if you do not wish to have any of your medical information sent to your physician, you can still participate in this research study.

Do you request that we send important medical findings from your study tests/exams to your personal physician?

[ ] Yes [ ] No _____ Initials

Participation in Genetic Studies

The genetic studies described are for research purposes only. Therefore, you will receive no results from this study (except as described above and in this section). It is not the purpose of this study to look for or provide you with any medical information or diagnoses relating to your present condition or any other disease or illness. The research tests are not being used as diagnostic tests for any disease or illness. Your participation in this study is not a substitute for your regular medical care or check-ups.

Through this research, we may find that you have an abnormal gene or gene product (RNA or protein) which indicates a risk for developing a disease at some time in the future. It is also possible that the research results may indirectly provide unexpected personal information about you or your family (such

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as ethnic/racial background or an unknown genetic relationship between family members). Please talk with the study doctor if you have any questions or concerns about the genetic testing being done in this research study. He/she may also refer you to a genetic counselor for further information.

It is possible that this study will identify information about you that was previously unknown, such as disease status or risk. There are no plans to provide this information to you or your physician.

HOW LONG WILL I BE IN THIS STUDY?
You will be asked to remain in the study from the screening period until your 30 day follow up visit, which is a total of 5 months. We would like to keep track of your medical condition for up to two years. Keeping in touch with you and checking on your condition helps us look at the long-term effects of the study.

You can choose to stop participating at any time without penalty or loss of any benefits to which you are entitled. However, if you decide to stop participating in the study, we encourage you to talk to your doctor first.

It is important to tell the study doctor if you are thinking about stopping so any risks from the study drugs can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you. The study doctor may stop you from taking part in this study at any time if she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

WHAT ARE THE RISKS OF THE STUDY?
Drugs used for anti-cancer therapy often have some undesirable side effects. It is important to be aware that there may be other side effects that are not yet known and cannot be foreseen. Side effects may go away after the study drug has stopped, but it is also possible that side effects may last a long time or forever. They may range from mild to life threatening or even lethal. It is possible that side effects can be minimized with additional treatments. Many side effects can be prevented or minimized by noticing the side effects early while they are still mild. Therefore, it is important to tell the study doctor or study nurse immediately about any changes in health that may have occurred even if you do not think they are related to the study. Your study doctor may give you treatment to help control side effects. If your study nurse or study doctor explains how to apply some preventative measures (for example to reduce risk of skin toxicity) please listen carefully. As a result of your participation in this study, you are at risk for the following side effects. You should discuss these with the study doctor and your regular health care provider if you choose.

As of 26 October 2021, more than 7,416 people have received talimogene laherparepvec with approximately 1,479 subjects having received talimogene laherparepvec in research studies and approximately 5,937 patients were prescribed talimogene laherparepvec (IMLYGIC®) after it was approved for sale.

Side effects that other people have had in research studies that are thought to have been caused by talimogene laherparepvec are:

Very Common Side Effects ***(may affect more than 1 person in 10)***

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- Flu like illness: chills, fever, feeling tired, muscle pain, nausea and vomiting
- Injection site pain
- Headache
- Joint pain
- Arm or leg pain
- Diarrhea
- Constipation

Common Side Effects ***(may affect between 1 and 10 people in every 100)***

- Injection site reactions: bleeding, redness, swelling, inflammation
- Skin infection caused by bacteria at the site of injection: symptoms may include fever, chills, redness or swelling at the injection site or the site of the tumor, and may require hospitalization for antibiotic treatment
- Wound complication at the injection site (secretion or discharge)
- Pain: pain after procedure, in the tumor, in the abdomen, throat pain, pain in the armpit or groin
- Abdominal discomfort
- Cold sore or fever blister in mouth (Oral herpes)
- Low red blood cell count (Anemia)
- Not feeling well (Malaise)
- Weight loss
- Dehydration
- Bruise
- Dizziness
- Skin or face becomes warm and reddened (Flushing)
- Rash
- Inflamed skin (Dermatitis)
- Blood clot (Deep vein thrombosis)
- Autoimmune Reactions: (a reaction of your body's immune system fighting your body's own tissues) have been reported in some patients administered talimogene laherparepvec. Examples of autoimmune reactions that have been reported in patients receiving talimogene laherparepvec include:
    - Inflammation of the kidneys (glomerulonephritis)
    - Inflammation of the blood vessels (vasculitis)
    - Inflammation of the lungs (pneumonitis)
    - Areas of skin with loss of color (vitiligo)
    - If you already have psoriasis (itchy, flaky patches or scaling of the skin), it may get worse

  It is possible that an autoimmune reaction could occur in any part of the body. Please tell your doctor if you have had any type of autoimmune disease before administration of talimogene laherparepvec, and all treatments you are receiving for the disease.

Uncommon Side Effects ***(which may affect between 1 and 10 people in every 1000)***

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- Injection site reactions: warmth, incision site infection
- Eye infection caused by herpes virus (Herpetic keratitis)
- Difficulty breathing: People receiving talimogene laherparepvec have experienced difficulty breathing or the sensation of shortness of breath. In addition, if you have a tumor in your neck, your doctor may warn you that you might experience compression of your airways while receiving talimogene laherparepvec. This might require a surgical procedure on the neck to open a direct airway. This occurred in a talimogene laherparepvec treated patient who had a similar problem before treatment. A tube might need to be inserted into the opening in your throat. This tube may be connected to a machine to help you breathe.
- Plasmacytoma (a collection of abnormal antibody-producing white blood cells) in the area where talimogene laherparepvec is injected. Plasmacytoma may be associated with multiple myeloma (a cancer of white blood cells affecting the bone marrow).
- Symptoms of delayed wound healing at or around the injection site such as injection site discharge, foul odor, or dead tissue at the injection site. If you notice symptoms of delayed wound healing at the injection site(s), especially if you have risk factors such as diabetes, poor blood circulation, have had radiation to the site, you should contact the study doctor or his/her study staff immediately.

Injection Site Reactions – Reactions at or near the area of the injection have been seen in other people administered talimogene laherparepvec. Symptoms include bleeding, redness, swelling and inflammation of the injection site. Skin infection caused by bacteria at the site of injection which may require hospitalization for antibiotic treatment have also been reported. Other symptoms may include warmth at the injection site or symptoms of delayed wound healing at or around the injection site such as injection site discharge, foul odor, or dead tissue at the injection site. If you notice symptoms of delayed wound healing at the injection site(s), you should contact the study doctor or his/her staff immediately.

Side Effects with Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF) – Talimogene laherparepvec contains genetic material that makes human GM-CSF. Human GM-CSF is a medicine used to treat patients with blood cell counts that are all low. Known side effects of human GM-CSF include, but are not limited to, musculoskeletal pain, fever, chills, shortness of breath, rash, fatigue, gastrointestinal effects, and fluid around heart and lungs. Although the amount of human GM-CSF released when treating tumor lesions with talimogene laherparepvec is very small, these side effects may still occur and your doctor will be looking for them.

Transmission of Talimogene Laherparepvec – You should always observe proper hygiene (wash your hands with warm water and soap after touching your injected lesions or injected sites or handling the dressings) to avoid potentially spreading talimogene laherparepvec to other persons.

Herpetic infections have been reported in close contacts or family members of subjects receiving talimogene laherparepvec. TVEC could potentially spread to your family members or other close contacts (household members, care-givers, sex partners, or someone you share a bed with) at any time after your tumor(s) are injected with the study drug. This may occur if your family member or other close contact touches the injection site or has contact with your body fluids or with the inside of the dressing(s) covering your injection site(s).

Spreading TVEC may be more likely if your close contact has a break in the skin or mucous membranes that comes into contact with your injection site or your body fluids. In patients treated with TVEC in clinical trials, TVEC has been found on the surface of the injected tumors, and on the outside of the dressings that covered these injection sites.

Talimogene laherparepvec have also been detected in patients' blood and urine, and in the patient's mucous membranes of the mouth and genitals, no samples had detectable talimogene laherparepvec 30 days after the end of treatment. For patients who had talimogene laherparepvec presence in the surface of injected tumors, no samples had detectable talimogene laherparepvec 60 days after end of treatment.

If a close contact has been exposed to TVEC, it is possible that they could develop symptoms similar to that of a herpes virus infection (see below). However, the chance of this happening is low due to the changes in TVEC that make it different from the naturally occurring herpes simplex virus, but you should know how to recognize these symptoms. Please contact the study doctor or study staff if a close contact develops herpes virus infection symptoms.

Most adults in the population have been exposed to the naturally occurring herpes simplex (also known as "cold sore") virus (HSV-1). Common signs and symptoms of the naturally occurring herpes simplex virus include:

- Sores around the mouth ("cold sore", "fever blister") or the genitals ("genital sore").
- Blisters may develop on the fingers, ears, or face.
- Eye infection (herpetic keratitis) with eye pain, light sensitivity, discharge from the eyes or blurry vision.
- Abdominal pain and infections, and inflammation inside the abdomen (infrequently).
- Rarely, serious infections of the brain (encephalitis) or spinal cord, causing paralysis (unable to move) have been reported. Signs may include fever, confusion or other behavior changes, headache, numbness and pain in the legs, constipation, or difficulty with urination.
- Life-threatening infections (disseminated herpes) can develop in people with a weakened immune system.
    - Disseminated herpes is a type of herpes infection that has spread to other parts of the skin and internal organs.

After infection, the naturally occurring herpes virus may travel to spinal nerve roots. The virus can reactivate from the nerve roots and cause recurrent cold sores or other signs of infection as described above. Stress, other illness, or menstruation are common triggers for reactivation of the naturally occurring virus.

Signs and symptoms of infection with TVEC could be similar to those described above, although TVEC has been changed to reduce the chance of this happening.

Delay in Response with TVEC Administration – Given that TVEC may help by stimulating your immune system (immunotherapy), it is possible that there can be a delay in your body

responding to the study drug. In addition, you may also see an increase in the size of existing tumors and/or the development of new tumors before potentially seeing a response to TVEC.

Allergic Reactions – As with any medication, you may have an allergic reaction to TVEC. Symptoms of an allergic reaction in general may include headache, rash, itching, flushing, swelling, shortness of breath, nausea and sometimes vomiting. Severe allergic reactions can cause dizziness, severe skin reactions, difficulty breathing or swallowing, a decrease in blood pressure, and could be life threatening. If you have symptoms of an allergic reaction, you should contact the study doctor or his/her study staff immediately. If you have had an allergic reaction to TVEC or any of its ingredients, you should inform your doctor.

Reproductive Risks
For women: The effects of the study drug on a developing pregnancy are not well understood, although herpes viruses are known to cause complications during pregnancy. Women who are pregnant or breastfeeding are excluded from this study.

If you are a woman who could possibly become pregnant (you have not completed menopause, or you have not had a hysterectomy and/or both tubes and/or both ovaries removed), and you have a partner who is able to father children, a blood pregnancy test will be done (using 1 teaspoon of blood drawn from a vein by needle-stick), and it must be negative before you can continue in this study. In women 40 years old and older, blood pregnancy tests can sometimes give a false positive or indeterminate result, and additional testing may be required.

You and your partner must agree to either abstain completely from vaginal intercourse for the duration of this study and for 90 days after the last dose of study drug, or agree to use highly effective methods of contraception for the same length of time. Due to unknown risks and potential harm to the unborn fetus, sexually active women of childbearing potential must use a reliable method of birth control while participating in this study. Reliable methods of birth control are: abstinence (not having sex), oral contraceptives, OrthoEvra patch, NuvaRing, intrauterine devices (IUD), Nexplanon implant, DepoProvera, tubal ligation, or vasectomy of the partner (with confirmed negative sperm counts) in a monogamous relationship (same partner). An acceptable, although less reliable, method involves the careful use of condoms and spermicidal foam or gel and/or a diaphragm with spermicide with Plan B used for any noticed condom or diaphragm failures. We encourage you to discuss this issue further with your physicians if you have any questions.

For men: Your participation in this research study may damage your sperm, which could cause harm to a child that you may father while on this study. Such harm may be currently unforeseeable. If you are sexually active, you must agree to use a medically acceptable form of birth control in order to be in this study and for (specify period of time following study participation if applicable) months afterwards. Medically acceptable contraceptives include: (1) surgical sterilization (such as a vasectomy), or (2) a condom used with a spermicide. Contraceptive measures such as Plan B (TM), sold for emergency use after unprotected sex, are not acceptable methods for routine use. You should inform your partner of the potential for harm to an unborn child. She should know that if pregnancy occurs, you will need to report it to the study doctor, and she should also promptly notify her doctor.

Risks of Drawing Blood:

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Risks associated with drawing blood from your arm include momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or fainting are also possible, although unlikely.

Risk of CT Scan:
Computed Tomography (CT) is a way to make x-ray images of the inside of the body. The CT scanner is a doughnut-shaped machine that uses x-rays to create computer pictures that show structures inside your body more clearly than regular x-ray pictures. During the procedure, a technologist will take you into the CT scan room where you will lie down on the subject table (usually on your back) inside of the CT machine. You should get comfortable because it is very important that you not move during certain parts of the test.

CT examinations differ depending on the part of your body being studied. For example, if your abdomen is being studied, a series of pictures will be taken from your lower chest to your lower pelvis. During the study, you will be asked to hold your breath so that the pictures will not be blurred. The machine will make some noise, and the table will move during the scan. Also, you may receive signals from the technologist or from the machine about your breathing. Before or during the study, you may be given an injection of contrast liquid in your vein to allow the radiologist to obtain clearer images of your organs. If you have any discomfort during the test or after the injection, be sure to tell the technologist.

Risk of MRI Scan:
Magnetic resonance imaging (MRI) uses a magnet and radio waves to make diagnostic medical images of the body. There have been no ill effects reported from exposure to the magnetism or radio waves used in this test. However, it is possible that harmful effects could be recognized in the future. A known risk is that the magnet could attract certain kinds of metal. Therefore, we will carefully ask you about metal within your body (this includes certain dyes found in tattoos). If there is any question about potentially hazardous metal within your body, you will not be able to have an MRI.

If you have an MRI as part of your tumor assessment, you will enter a large room in which a magnet is present. You will be placed on a narrow bed and then slide into a small tunnel approximately 6 feet in length and 25 inches in diameter. You will be asked to lie still for about one hour on this bed. You will hear a loud machine-like noise. You may be asked to have a harmless monitoring device applied during the study. During the study, you can have voice contact and physical contact with someone in attendance if you desire.

Risks of Radiation:
You will have a number of CT scans or MRI scans that are part of the regular care for your condition, and you would have them whether or not you participate in this research. These studies will not add to the risk due to participating in the research. However, if you have concerns about the overall radiation exposure or MRI safety issue, you should discuss them with your physician.

Sometimes subjects have allergic reactions to the dyes used in imaging scans. This is rare. It can involve itching or rash. In severe cases, you may have difficulty breathing and dangerous lowering of your blood pressure. If you know that you have an allergy to the dye, or to iodine or shellfish, please let your study doctor and radiologist know.

Risks of Peritoneal Catheter:

There are several risks associated with the use of a peritoneal catheter.
The risk of **bowel perforation** is less than 1%, and it usually occurs during entry into the abdominal cavity or when the catheter and stylet (probe) are moved further into the abdomen. Surgical exploration is necessary with repair of the perforation and removal of the catheter.

Bleeding is rarely a significant problem after peritoneal catheter placement. This typically does not require medical intervention outside of holding pressure at the exit site.

Wound infection is uncommon and often can be treated with antibiotics when it is on the surface. If the wound is deeper, then it may need to be drained surgically.

Outflow failure may be due to several causes including clots or fibrin (protein) in the catheter, a kink in the tunnel under the skin, placement of the catheter in the omentum (organ above the intestines), blockage from omentum, or adhesions (scar-like tissues). A number of treatments might be required including flushing with a clot dissolving agent and repositioning of the catheter.

Leakage of the infusion solution may be identified by the presence of drainage at the exit site or the appearance of a bulge underneath the catheter site. An x-ray study of the catheter will determine the method of treatment that is pursued.

Risk of Peritoneal Catheter – TVEC Administration:
In this study, TVEC will be administered into the peritoneum via intraperitoneal catheter. Since this administration method is different than the approved method of administering the drug normally, there may be additional associated risks. These include:

- Ileus (the inability of the intestine (bowel) to contract normally and move waste out of the body)
- Bowel perforation (rupture) due to tumor response
- Peritonitis (inflammation of the membrane lining the abdominal wall and covering the abdominal organs)

Drug and Food Interactions:
For your safety, you must tell the study doctor or nurse about all the prescribed medical foods and drugs, herbal products, over-the-counter (OTC) drugs, vitamins, natural remedies, and alcohol that you are taking before you start the study and before starting to take any of these products while you are on the study.

Potential Risks of Genetic Testing and the Genetic Information Non-Discrimination Act (GINA):
There is a potential risk of loss of confidentiality. Every effort will be made to protect your confidential information, but this cannot be guaranteed. The genetic information obtained as a result of your participation in this research will not be included in your medical record. Information from which you may be personally identified will be maintained in a confidential, secure location at DUHS, accessible only by authorized members of the study team, and you will not be disclosed to third parties except as described in this consent form, with your permission, or as may be required by law.

The Genetic Information Nondiscrimination Act (GINA) is a Federal law that will protect you in the following ways:
-Health insurance companies and group plans may not request genetic information from this research

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-Health insurance companies and group 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 when making a decision to hire, promote, or fire you or when setting the terms of your employment.

GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

There may be risks, discomforts, drug interactions or side effects that are not yet known.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?
If you agree to take part in this study, the investigational study drug may or may not help control your cancer. This may or may not make you feel better or live longer. We hope that in the future the information learned from this study will benefit other people with your condition. If proven effective, TVEC may be developed into a new therapeutic approach for treating human peritoneal surface dissemination of gastrointestinal and ovarian cancers.

WHAT ALTERNATIVES ARE THERE TO PARTICIPATION IN THIS STUDY?
Your other choices may include the following:

- Getting treatment or care for your cancer without being in a study
- Depending on the therapies that you have already received, there may be other potentially beneficial approved treatments available for your cancer. These treatments may shrink tumors, delay progression of cancer, provide symptom relief, or prolong your life and could include chemotherapy (for example, platinum-based chemotherapy) or drugs that target a specific abnormality in some cancers. You should discuss these options with your doctor.
- Taking part in another study.
- Getting no treatment
- Getting comfort care (also called palliative care) only. This type of care helps reduce pain, tiredness, appetite problems, and other problems caused by the cancer. It does not treat the cancer directly.

Talk to your doctor about your choices, including the risks and benefits of each choice, before you decide if you will take part in this study.

WILL MY INFORMATION BE KEPT CONFIDENTIAL?
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 unless it is authorized by you, required by law, or necessary to protect the safety of yourself or others. There is always some risk that even de-identified information might be re-identified.

Participant 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.

WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you and/or information we get from your medical records or other facilities about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes**:** demographics, medical and cancer history, concomitant medications, physical exam, abdominal measurement, height, vital signs and weight, blood tests, a serum pregnancy test (if applicable), tumor assessment that includes a CT and/or MRI of the chest, abdomen, and pelvis, and information about your archived tumor tissue (if applicable).

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study will be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with Medical Center operations.

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer.

Your personal health information and information that identifies you ("your health information") may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from government agencies such as the Food and Drug Administration (FDA) or the Office of Human Research Protections (OHRP), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable.

Monitors, auditors, IRB or other regulatory agencies will be granted direct access to the participant's original medical record for verification of clinical trial procedures or data, without violating confidentiality of the participant and to the extent permitted by other applicable laws.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state privacy rules.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for an indeterminate period of time. This authorization does not expire. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities

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in the study are completely finished.

You can tell Edward Levine, MD that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Edward Levine, MD
Medical Center Blvd
Wake Forest Baptist Medical Center
Winston-Salem, NC 27157

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form you give us permission to use your Protected Health Information for this study.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a clinical trial. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

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

Laboratory test results and other clinically relevant medical reports created as a result of your participation in the research study may be entered into the computer systems of Wake Forest University Health Sciences and North Carolina Baptist Hospital. These will be kept secure, with access to this information limited to individuals with proper authority, but who may not be directly involved with this research study.

A North Carolina Baptist Hospital (NCBH) medical record will be created for all study participants. Information about your participation in the study will be placed in the NCBH medical record, along with any routine medical test results that were obtained at NCBH as part of this study.

WHAT ARE THE COSTS TO YOU?

All study costs, including any study medications and procedures related directly to the study, will be paid for by the study. Costs for your regular medical care, which are not related to this study, will be your own responsibility.

Amgen will provide the study drug free of charge to you.

The catheter placement will be paid for by the study.

Parking validation will be provided for all study-related visits.

WHAT ABOUT COMPENSATION?
You will not receive any monetary compensation for your participation in this study.

WHAT ABOUT RESEARCH RELATED INJURIES?
Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest University School of Medicine, and the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at (336) 716-3467.

There is no commitment by Duke University, Duke University Health System, Inc., Duke physicians, or the study supporter, Amgen, Inc. to provide monetary compensation or free medical care to you in the event of a study-related injury.

This Study also requires ICH-GCP compliance.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?
For questions about the study or a research-related injury, or if you have problems, concerns, questions or suggestions about the research, contact Edward Levine, MD at (336) 713-5440 during regular business hours and at (336) 713-5440 after hours and on weekends and holidays and ask that he be paged.

For questions about your rights as a research participant, or to discuss problems, concerns or suggestions related to the research, or to obtain information or offer input about the research, contact the Chairman of the IRB at (336) 716-4542 or the Research Subject Advocate at (336) 716-8372.

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?
Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be because it is in your best medical interest, your condition worsened, new information becomes available, you had an unexpected reaction, you failed to follow instructions, or because the entire study has been stopped. Information that identifies you may be removed from the data or specimens that are collected as part of this study and could be used for future research or shared with others without additional consent.

WFU School of Medicine
Institutional Review Board
IRB Number: IRB00056815
Meeting Date Approved 12/12/2022
Version Valid Until: 9/20/2023

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

STATEMENT OF CONSENT

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Subject Name (Printed):_____

Subject Signature: _____ Date: _____Time:_____ am pm

Person Obtaining Consent (Printed):_____

Person Obtaining Consent:_____ Date:_____ Time:_____ am pm

WFU School of Medicine
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