Study Title for Study Participants: Testing the combination of talimogene laherparepvec and pembrolizumab in patients with advanced melanoma who have progressed on anti-PD-1/L1 therapy

Official Study Title for Internet Search on http://www.ClinicalTrials.gov:
S1607, "A Phase II Study of Combining Talimogene Laherparepvec (T-VEC) (NSC-785349) and MK-3475 (pembrolizumab) (NSC-776864) in Patients with Advanced Melanoma Who Have Progressed on Anti-PD1/L1 Based Therapy"

What is the usual approach to my advanced melanoma?

You are being asked to take part in this research study because you have melanoma which has grown or has come back after receiving anti-PD1 or anti-PDL1 therapy. People who are not in a study are usually treated with either surgery, radiation, or with other FDA approved drugs. Sometimes, combinations of these treatments are used and your doctor can explain which may be best for you. These treatments can reduce symptoms and may stop the tumor from growing for several months or more.

What are my other choices if I do not take part in this study?

If you decide not to take part in this study, you have other choices. For example:

- you may choose to have the usual approach described above
- you may choose to take part in a different study, if one is available
- or you may choose not to be treated for cancer, but you may want to receive comfort care to relieve symptoms.

Why is this study being done?

The purpose of this study is to test any good and bad effects of the combination of study drugs called MK-3475 (pembrolizumab) and talimogene laherparepvec (T-VEC). This investigational approach could shrink your cancer, but it could also cause side effects. Researchers hope to learn if the combination of study drugs will shrink the cancer by at least 30% compared to its present size for at least a six month period in more than twenty percent of patients. MK-3475 (pembrolizumab) and talimogene laherparepvec (T-VEC) have already been FDA-approved to treat melanoma. They have not been tested together for melanoma. There will be about 64 people taking part in this study.

What are the study groups?

All study participants will get the same study treatment. It will include injection of talimogene laherparepvec (T-VEC) into your tumors that are injectable by your study doctor every 3 weeks. You will also receive MK-3475 (pembrolizumab) through a vein over a 30 minute period once every three weeks. This three week period is called a "cycle" and you will receive 36 cycles of this treatment.

How long will I be in this study?

You will receive the study drugs for up to two years. After you finish the study treatment, your doctor will continue to watch you for side effects and follow your condition for 10 years from the time you started study.

Because this study involves talimogene laherparepvec (T-VEC), an engineered virus (gene transfer agent) that is used to treat your melanoma, you will be asked to allow the study doctors to contact you for additional long-term follow-up so that the National Institutes of Health can monitor the long-term safety and effectiveness of talimogene laherparepvec (T-VEC). If this additional follow-up results in any additional findings, you will be informed. When you finish the study treatment, your treating physician will ask you for a phone number and address, so that the study doctors may continue to contact you via phone to follow-up on your status until 10 years after the time of your enrollment to the study.

What extra tests and procedures will I have if I take part in this study?

Most of the exams, tests, and procedures you will have are part of the usual approach for your cancer. However, there are some extra procedures that you will need to have if you take part in this study. One of the main reasons for doing this study is to examine your cancer tissue to see the amount of immune infiltration. Another important goal is to look at your blood to see how your immune system is working.

If you consent, small piece of cancer tissue that was removed from a previous biopsy will be taken at the beginning of the study if this cancer tissue is available to your treating physician. Since this biopsy has already been performed, there are no physical risks related to this "archival" tissue submission. Neither you nor your health care plan/insurance carrier will be billed for the collection or submission of the tissue that will be used for this study.

This study requires that the tissue be sent to a central laboratory for determination of a biomarker called "CD8 cell infiltration". (A biomarker can be a genetic feature or specific protein found in the tumor sample.) The "CD8 cells" will be compared over time. Therefore, small pieces of cancer tissue removed by biopsy will be taken for the study before you begin the study drugs and at 4 weeks after starting the study drugs. These samples are required in order for you to take part in this study because the research on the samples is an important part of the study. The

researchers will also request an optional biopsy (see "Additional Studies" section below) if your disease gets worse (progresses) within 5 years after you start the required study treatment. This will be used to compare to the required tissue samples. The research biopsy is done in a similar way to biopsies done for diagnosis.

Although optional, we ask that you have a biopsy done if the cancer gets worse and that tissue from this biopsy also be sent to the central laboratory. If there is leftover tissue, the study would like to store it for future research. This will be discussed in the "Additional Studies" section.

Common side effects of a biopsy are a small amount of bleeding at the time of the procedure, pain at the biopsy site, which can be treated with regular pain medications, and bruising. Rarely, an infection can occur. You will sign a separate consent form before the biopsy is taken. This will be a standard surgical consent form from the institution where the biopsy procedure takes place.

A blood sample will be taken for the study before you begin the study drugs, 2 weeks after starting the study drugs, 4 weeks after starting the study drugs, 9 weeks after starting the study drugs, and if your cancer gets worse. These samples will be collected at the same time you have blood collected for laboratory tests. They are required in order for you to take part in this study because the research on the samples is an important part of the study. This is not part of regular cancer care, but is being done as part of this research study. If there is leftover blood, the study would like to store it for future research. This will be discussed in the "Additional Studies" section.

Your test results will be identified by a unique code and the list that links the code to your name will be kept separate from your sample and health information. You and your study doctor will not receive the results of these tests.

Neither you nor your health care plan/insurance carrier will be billed for the collection or submission of the tissue and blood that will be used for this study.

What possible risks can I expect from taking part in this study?

If you choose to take part in this study, there is a risk that talimogene laherparepvec (T-VEC, IMLYGIC) may not be as good as the usual approach for your cancer or condition at shrinking or stabilizing your cancer.

You may also have the following discomforts:

- **Spend more time in the hospital or doctor's office than usual**
- **Be asked sensitive or private questions about things you normally do not discuss**
- **May not be able to take part in future studies**
- **There is a risk someone could get access to the personal information in your medical records or other information researchers have kept about you. Someone might be able to trace this information back to you. The researchers believe the chance that**

someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information. In some cases, this information could be used to make it harder for you to get or keep a job. There are laws against misuse of genetic information, but they may not give full protection. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

- **There can also be a risk in finding out new genetic information about you. New health information about inherited traits that might affect you or your blood relatives could be found during a study.**

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

There is also a risk that you could have side effects from the study drugs.

Here are important things to know about side effects:

- **The study doctors do not know who will or will not have side effects.**
- **Some side effects may go away soon, some may last a long time, and some may never go away.**
- **Some side effects may make it hard for you to have children.**
- **Some side effects may be mild. Other side effects may be very serious and even result in death.**

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:

- **If you notice or feel anything different, tell the study doctor. He or she can check to see if you are having a side effect.**
- **The study doctor will work with you to treat some side effects.**
- **The study doctor may adjust the study drugs to try to reduce side effects.**

The tables below show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Possible Side Effects of MK-3475 (pembrolizumab):

COMMON, SOME MAY BE SERIOUS In 100 people receiving MK-3475 (pembrolizumab), more than 20 and up to 100 may have:
• **Tiredness**

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving MK-3475 (pembrolizumab), from 4 to 20 may have:

- **Nausea**
- **Infection**
- **Loss of appetite**
- **Pain in back**
- **Joint stiffness**
- **Cough**
- **Swelling and redness of the skin**

MK-3475 (pembrolizumab) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- **Anemia which may require blood transfusion**
- **Pain in lymph nodes**
- **Blood clot which may cause bleeding, confusion, paralysis, seizures and blindness**
- **Hormone gland problems (especially the thyroid, pituitary and adrenal glands, and pancreas). Signs and symptoms may include: headaches that will not go away or unusual headaches, extreme tiredness or changes in mood or behavior; decreased sex drive; weight loss or weight gain; excessive thirst or urine; dizziness or fainting**
- **Intestinal problems (colitis) that can rarely lead to tears or holes in your intestine. Signs and symptoms of colitis may include: diarrhea or increase in bowel movements, blood in your stools or dark, tarry, sticky stools, severe belly pain or tenderness**
- **Diarrhea**
- **Sores in the mouth which may cause difficulty swallowing**
- **Pain in belly**
- **Sores in the bowels**
- **Chills, fever**
- **Liver problems (hepatitis) which can cause liver failure. Signs and symptoms of hepatitis may include: yellowing of your skin or the whites of your eyes, severe nausea or vomiting; drowsiness; pain in the right upper belly**
- **Pain or swelling of the joints**
- **Problem of the muscle, including swelling, which can cause muscle pain and severe muscle weakness sometimes with dark urine**
- **Fluid in the joints**
- **Pain in chest**
- **Lung problems (pneumonitis and other conditions). Symptoms may include: new or worsening cough, chest pain, shortness of breath.**

- **Skin: itching; acne; rash (can be severe); blisters and peeling on the skin, mouth; skin changes; hives**

RARE, AND SERIOUS

In 100 people receiving MK-3475 (pembrolizumab), 3 or fewer may have:

- **Feeling of "pins and needles" in arms and legs**
- **Redness, pain or peeling of palms and soles**

MK-3475 (pembrolizumab) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- **Heart problems including swelling and heart failure. Symptoms and signs of heart problems may include: Shortness of breath, swelling of the ankles and body.**
- **Swelling and redness of the eye**
- **Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat**
- **Reaction during or following a drug infusion which may cause fever, chills, rash**
- **Damage to organs in the body when donor cells attack host organs which may cause yellowing of eyes and skin, itchy dry skin**
- **Damage to organs in the body when the body produces too many white cells**
- **A condition with high blood sugar which leads to tiredness, frequent urination, excessive thirst, headache, nausea and vomiting, and can result in a coma**
- **Problem of the nerves that can cause paralysis. Signs and symptoms may include: numbness, tingling of hands and feet; weakness of the arms, legs.**
- **Swelling of the brain (encephalitis/meningitis) which may cause headache, confusion, sleepiness, seizures, and stiff neck**
- **Kidney problems, including nephritis and kidney failure requiring dialysis. Signs of kidney problems may include: decrease in the amount of urine, blood in your urine, ankle swelling.**
- **Swelling or tenderness of blood vessels**

Possible side effects of talimogene laherparepvec (T-VEC)

COMMON, SOME MAY BE SERIOUS

In 100 people receiving talimogene laherparepvec (T-VEC, IMLYGIC), more than 20 and up to 100 may have:

- **Nausea, vomiting**
- **Flu-like symptoms including chills, fever, tiredness, body aches**
- **Injection site reactions including swelling, redness or bleeding**

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving talimogene laherparepvec (T-VEC, IMLYGIC), from 4 to 20 may have:
• **Anemia which may require blood transfusion** • **Pain at injection sites, the tumor sites, armpit or groin** • **Pain in the throat** • **Constipation, diarrhea** • **Eye infection caused by herpes virus** • **Cold sore or blister in the mouth** • **Infection at the injection sites** • **Non-healing wound or delayed wound healing** • **Weight loss, loss of appetite** • **Dehydration** • **Dizziness, headache** • **Itching, rash** • **Swelling and redness of the skin** • **Patches of skin with loss of color** • **Flushing** • **Blood clot which may cause swelling, pain, shortness of breath**

RARE, AND SERIOUS In 100 people receiving talimogene laherparepvec (T-VEC, IMLYGIC), 3 or fewer may have:
• **Activation of the immune system against body's own tissue, which may cause injury to the kidneys, lungs, blood vessels, or other organs** • **Malignant tumor (plasmacytoma) that grows at injection site** • **Blockage of the airway** • **Massive bleeding from tumors in patients with head and neck cancers receiving radiation and T-VEC injections in the tumor**

Other possible side effects of T-VEC:

- **Pain in your muscles and/or joints**
- **Shortness of breath**
- **Tiredness**
- **Fluid around your heart and/or lungs**
- **Allergic reaction. Symptoms of an allergic reaction include headache, rash, itching, flushing, swelling, shortness of breath, nausea, vomiting, dizziness, severe skin reactions, difficulty breathing or swallowing, and a decrease in blood pressure. Severe allergic reactions could be life threatening. If you have symptoms of an**

allergic reaction, contact the study doctor or the study staff right away and/or visit your local emergency room.

- **You may see an increase in the size of your tumors and/or the development of new tumors before the T-VEC starts working.**

<u>Information about potential transmission of talimogene laherparepvec (T-VEC) to Close Contacts and Family Members</u>

Can talimogene laherparepvec (T-VEC) be spread to my family members or other close contacts and how long after treatment is this possible? There have been no reported cases of spreading of talimogene laherparepvec (T-VEC) to close contacts or family members in clinical trials to date. However talimogene laherparepvec (T-VEC) 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 talimogene laherparepvec (T-VEC) 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 talimogene laherparepvec (T-VEC) in clinical trials, talimogene laherparepvec (T-VEC) has been found on the surface of the injected tumors, into the second week after the injection, but not on the outside of the dressings that covered these injection sites. Small amounts of talimogene laherparepvec (T-VEC) have been detected in patients' blood and urine for up to 1 week after injection. A study is ongoing to determine if talimogene laherparepvec (T-VEC) can be detected in mucous membranes of the mouth and genitals.

Is there any risk to my family members or other close contacts if they are exposed to talimogene laherparepvec (T-VEC)?

If a close contact has been exposed to talimogene laherparepvec (T-VEC), it is possible that they could develop symptoms of a herpes type infection (see below). However, the chance of this happening is low due to the changes in talimogene laherparepvec (T-VEC) that make it different from the naturally occurring herpes simplex virus, but you should know how to recognize these symptoms.

Symptoms that may be related to the naturally occurring herpes simplex virus type 1 (HSV-1):

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, and 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. A weakened immune system means your body has trouble protecting itself against infections, it can be caused by illness or some medications.**

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 talimogene laherparepvec (T-VEC) could be similar to those described above, although talimogene laherparepvec has been changed to reduce the chance of this happening.

What to do if you or a close contact develop any of the above symptoms:

- **You should report any signs or symptoms to your study doctor right away and you should ask your close contact to call their doctor for evaluation and appropriate treatment.**
- **You or your close contact may be asked to come to the clinic for a test that may be able to determine if these symptoms may be due to talimogene laherparepvec (T-VEC).**
- **This test is likely to be most reliable if it can be performed in the first 3 days after symptoms develop.**

Who Should Not Have Contact with talimogene laherparepvec (T-VEC)? Persons with severely weakened immune systems should not be treated with talimogene laherparepvec (T-VEC) as they may be at increased risk for serious, life-threatening herpetic infections after receiving talimogene laherparepvec (T-VEC). Tell your doctor if you have a weakened immune system.

If your close contact or family member is pregnant or has a weakened immune system, they should not touch injection sites, change your dressings or clean your injection sites. Keep used dressings and cleaning materials away from pregnant women, newborns, and those with weakened immune systems.

Are there any precautions I should take to prevent spread of talimogene laherparepvec (T-VEC) to others?

- **Avoid touching or scratching the injection site.**
- **Injection sites should be covered for at least 7 days after the last injection with watertight dressings which allow for air exchange. If the dressing comes loose or falls off prior to 7 days after the injection, it should be replaced right away with a clean dressing. However, you may need to keep the dressing on longer if the lesions at the injection sites / injection sites are weeping or oozing.**
- **Place all used dressings and cleaning materials in a sealed plastic bag, and throw them away as household waste or return to the study site for disposal as you are instructed by the site staff.**
- **You should always observe proper hygiene (wash your hands with warm water and soap after touching your injected lesions or handling the dressings) to avoid potentially spreading talimogene laherparepvec (T-VEC) to other persons.**
- **Close contacts who are pregnant or who have a weakened immune system should not touch injection sites, change your dressings or clean your injection sites.**
- **If you participate in this study, your doctor and/or his staff will provide you with additional instructions for injection site care.**

What should I tell my close contacts while I am being treated with talimogene laherparepvec (T-VEC)?

- **Avoid direct contact with your injection sites and body fluids.**
- **Wear gloves while changing your dressings that cover your injected sites. If your close contacts are accidentally exposed to talimogene laherparepvec (T-VEC), they should clean the affected area on their body with soap and water and /or a disinfectant. If they develop signs or symptoms of herpes infection, ask them to call their doctor, and you should report this to your study doctor.**

Can talimogene laherparepvec (T-VEC) be transmitted through sexual contact? The naturally occurring herpes simplex virus (HSV-1) can be transmitted through sexual contact. It is not known if talimogene laherparepvec (T-VEC) will behave the same way, thus you or your partner should use a latex condom during treatment and for up to 3 months after your last dose when engaging in sexual activity to prevent possible transmission of talimogene laherparepvec (T-VEC). For those with latex allergies, polyurethane condoms may be used.

Communicating these risks to family members and close contacts: talimogene laherparepvec (T-VEC) information sheets have been developed for close contacts and minors (individuals less than 18 years old) to inform them of these risks and the precautions. You will also receive detailed injection site care instructions. These documents will be provided to you by the study staff for you and for you to share with your close contacts once you have signed the consent form.

Risks of Venipuncture/Intravenous Needle Insertion:

Occasional, some may be serious: Mild pain and discomfort at the injection or needle insertion site as well as possible infection, bleeding, bruising, and soreness.

Rare: Severe pain, swelling, infection from the actual injection, and fainting.

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

Reproductive risks: You should not get pregnant, breastfeed, or father a baby while in this study. The drugs used in this study could be very damaging to an unborn baby. Check with the study doctor about what types of birth control, or pregnancy prevention, to use while in this study. Women of child bearing potential and men must agree to use adequate contraception (barrier method of birth control or abstinence) prior to study entry and for the duration of study participation through 3 months after receiving the last dose of treatment. If you become pregnant while receiving treatment on this study, you should inform your doctor immediately and stop the study drug.

What possible benefits can I expect from taking part in this study?

This study has only a small chance of helping you because we do not know if the study drug/study approach is effective. This study may help researchers learn things that may help other people in the future.

Can I stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

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

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study rules
- If the study is stopped by the sponsor, IRB or FDA.

What are my rights in this study?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

For questions about your rights while in this study, you may contact the Operations Office of the National Cancer Institute (NCI) Central Institutional Review Board (CIRB) at 888-657-3711.

What are the costs of taking part in this study?

The study drugs MK-3475 (pembrolizumab) and talimogene laherparepvec (T-VEC) will be supplied at no charge while you take part in this study. The cost of getting the study drugs ready and giving them to you is not paid for by the study sponsor so you or your insurance company may have to pay for this. It is possible that the MK-3475 (pembrolizumab) and talimogene laherparepvec (T-VEC) may not continue to be supplied to you while you are on the study. Although not likely, if this occurs, your study doctor will talk to you about your options.

You and/or your health plan/insurance company will need to pay for all of the other costs of treating your cancer while in this study, including the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no charge. Before you decide to be in the study, you should check with your health plan or insurance company to find out exactly what they will pay for.

You will not be charged for the research biopsy or blood draw required before you begin study treatment, during Week 4, or if your disease gets worse (progression).

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

What happens if I am injured or hurt because I took part in this study?

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. Contact information for your study doctor is listed on the consent cover page. The study sponsors will not offer to pay for medical treatment for injury. Your insurance company may not be willing to pay for study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a study.

No funds have been set aside to compensate you in the event of injury.

Who will see my medical information?

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- Montana Cancer Consortium
- The study sponsor, SWOG, Alliance, ECOG-ACRIN, NRG and any drug company supporting the study
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Institutional Biosafety Committee, IBC, a group of people who review research involving biological materials.
- National Institutes of Health (NIH) Office of Science Policy
- The Food and Drug Administration and the National Cancer Institute in the U.S., and similar ones if other countries are involved in the study.

Where can I get more information?

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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

Who can answer my questions about this study?

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact information for your study doctor is listed on the consent cover page.

ADDITIONAL STUDIES SECTION:

This section is about optional studies you can choose to take part in

This part of the consent form is about optional studies that you can choose to take part in. You will not get health benefits from any of these studies. The researchers leading this optional study hope the results will help other people with cancer in the future.

The results will not be added to your medical records and you or your study doctor will not know the results.

You will not be billed for these optional studies. You can still take part in the main study even if you say 'no' to any or all of these studies. If you sign up for but cannot complete any of the studies for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for each of the following studies.

Optional Biobanking for Possible Future Studies

Researchers are trying to learn more about cancer, diabetes, and other health problems. Much of this research is done using samples from your tissue, blood, urine, or other fluids. Through these studies, researchers hope to find new ways to prevent, detect, treat, or cure health problems.

Some of these studies may be about genes. Genes carry information about features that are found in you and in people who are related to you. Researchers are interested in the way that genes affect how your body responds to treatment.

If you choose to take part, tissue and blood that is leftover from the research studies will be stored in a biobank. The researchers ask your permission to store and use your samples and related health information (for example, your response to cancer treatment, results of study tests and medicines you are given) for medical research. The research that may be done is unknown at this time. Storing samples for future studies is called "biobanking". The Biobank is being run by SWOG and supported by the National Cancer Institute.

WHAT IS INVOLVED?

If you agree to take part, here is what will happen next:

1) If your disease gets worse (progresses) within 5 years after you start the study treatment, the researchers would like to collect about ½ inch of tissue. This would be collected at the time of a standard of care biopsy. It would be used for "mutational load" testing.
2) The researchers would like to keep any extra (remaining) tissue and blood that was collected for "mutational load" testing. The extra blood and tissue will be saved at the laboratory that performs the testing.

3) Your blood and tissue samples and some related health information may be stored in the Biobank, along with samples and information from other people who take part. The samples will be kept until they are used up. Information from your medical record will be updated from time to time.
4) Qualified researchers can submit a request to use the materials stored in the Biobanks. A science committee at the clinical trials organization, and/or the National Cancer Institute, will review each request. There will also be an ethics review to ensure that the request is necessary and proper. Researchers will not be given your name or any other information that could directly identify you.
5) Neither you nor your study doctor will be notified when research will be conducted or given reports or other information about any research that is done using your samples.
6) Some of your genetic and health information may be placed in central databases that may be public, along with information from many other people. Information that could directly identify you will not be included.

WHAT ARE THE POSSIBLE RISKS?

1) Common side effects of a biopsy are a small amount of bleeding at the time of the procedure, pain at the biopsy site, which can be treated with regular pain medications, and bruising. You will sign a separate consent form before the biopsy is taken. This will be a standard surgical consent form from the institution where the biopsy procedure takes place.
2) There is a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.
3) There is a risk that someone could trace the information in a central database back to you. Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.
4) In some cases, this information could be used to make it harder for you to get or keep a job or insurance. There are laws against the misuse of genetic information, but they may not give full protection. There can also be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a study. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

HOW WILL INFORMATION ABOUT ME BE KEPT PRIVATE?

Your privacy is very important to the researchers and they will make every effort to protect it. Here are just a few of the steps they will take:

1) When your sample(s) is sent to the researchers, no information identifying you (such as your name) will be sent. Samples will be identified by a unique code only.
2) The list that links the unique code to your name will be kept separate from your sample and health information. Any Biobank and SWOG staff with access to the list must sign an agreement to keep your identity confidential.

3) Researchers to whom SWOG sends your sample and information will not know who you are. They must also sign an agreement that they will not try to find out who you are.
4) Information that identifies you will not be given to anyone, unless required by law.
5) If research results are published, your name and other personal information will not be used.

WHAT ARE THE POSSIBLE BENEFITS?

You will not benefit from taking part.

ARE THERE ANY COSTS OR PAYMENTS?

There are no costs to you or your insurance. You will not be paid for taking part. If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

WHAT IF I CHANGE MY MIND?

If you decide you no longer want your samples to be used, you can call the study doctor, who will let the researchers know. Contact information for your study doctor is listed on the consent cover page. Then, any sample that remains in the bank will no longer be used and related health information will no longer be collected. Samples or related information that have already been given to or used by researchers will not be returned.

WHAT IF I HAVE MORE QUESTIONS?

If you have questions about the use of your samples for research, contact the study doctor. Contact information for your study doctor is listed on the consent cover page.

Please circle your answer to show whether or not you would like to take part in each option

Samples for the Laboratory Studies

I agree to have my samples collected and I agree that my sample(s) and related information may be used for the laboratory studies described above.

Yes **No**

Samples for Future Research Studies

My tissue and blood samples and related information may be kept in a Biobank for use in future health research.

Yes **No**

Future Contact

I agree to allow my study doctor, or someone approved by my study doctor, to contact me regarding future research involving my participation in this study.

Yes **No**

Signature:

This study has been explained to me, and I have been told what my enrollment in the study involves. I have read all pages of this consent and have had my questions answered to my satisfaction at this time. I consent to participate in this study and any additional studies where I circled 'yes'. I understand that by signing this form I have not given up any of my legal rights. I will be given a copy of this consent form. I may also request a copy of the protocol (full study plan).

Participant Signature: _____

Date: _____

Signature of Person Obtaining Consent: _____

Date: _____

Time of consent: _____ (AM) (PM)
(Required for initial consent only)

SPECIMEN CONSENT SUPPLEMENTAL SHEETS

How are Specimens Used for Research?

Where do specimens come from?

A specimen may be from a blood sample or from bone marrow, skin, toenails or other body materials. People who are trained to handle specimens and protect donors' rights make sure that the highest standards of quality control are followed by SWOG. Your doctor does not work for SWOG, but has agreed to help collect specimens from many patients. Many doctors across the country are helping in the same way.

Why do people do research with specimens?

Research with specimens can help to find out more about what causes cancer, how to prevent it, how to treat it, and how to cure it. Research using specimens can also answer other health questions. Some of these include finding the causes of diabetes and heart disease, or finding genetic links to Alzheimer's.

What type of research will be done with my specimen?

Many different kinds of studies use specimens. Some researchers may develop new tests to find diseases. Others may develop new ways to treat or even cure diseases. In the future, some of the research may help to develop new products, such as tests and drugs. Some research looks at diseases that are passed on in families (called genetic research). Research done with your specimen may look for genetic causes and signs of disease.

How do researchers get the specimen?

Researchers from universities, hospitals, and other health organizations conduct research using specimens. They contact SWOG and request samples for their studies. SWOG reviews the way that these studies will be done, and decides if any of the samples can be used. SWOG gets the specimen and information about you from your hospital, and sends the specimen samples and some information about you to the researcher. SWOG will not send your name, address, phone number, social security number or any other identifying information to the researcher.

Will I find out the results of the research using my specimen?

You will not receive the results of research done with your specimen. This is because research can take a long time and must use specimen samples from many people before results are known. Results from research using your specimen may not be ready for many years and will not affect your care right now, but they may be helpful to people like you in the future.

Why do you need information from my health records?

In order to do research with your specimen, researchers may need to know some things about you. (For example: Are you male or female? What is your race or ethnic group? How old are you? Have you ever smoked?) This helps researchers answer questions about diseases. The information that will be given to the researcher may include your age, sex, race, diagnosis, treatments and family history. This information is collected by your hospital from your health record and sent to SWOG. If more information is needed, SWOG will send it to the researcher.

Will my name be attached to the records that are given to the researcher?

No. Your name, address, phone number and anything else that could identify you will be removed before they go to the researcher. The researcher will not know who you are. How could the records be used in ways that might be harmful to me?

If your confidential genetic information is discovered, you may suffer from genetic discrimination. Genetic discrimination occurs if people are treated unfairly because of differences in their genes that increase their chances of getting a certain disease. In the past, this could have resulted in the loss of health insurance or employment. Because of this, The Genetic Information Nondiscrimination Act of 2008, also referred to as GINA, was passed by Congress to protect Americans from such discrimination. The new law prevents discrimination from health insurers and employers. This act was signed into federal law on May 21, 2008, and went into effect May 2009. This law does not cover life insurance, disability insurance and long-term care insurance.

While this study has safeguards in place to protect your confidential genetic information and to make it extremely unlikely that your identity would be connected with any special studies that are performed on your tissue, it is possible that this information could be discovered by someone who is unauthorized to have access to it.

How am I protected?

SWOG is in charge of making sure that information about you is kept private. SWOG will take careful steps to prevent misuse of records. Your name, address, phone number and any other identifying information will be taken off anything associated with your specimen before it is given to the researcher. This would make it very difficult for any research results to be linked to you or your family. Also, people outside the research process will not have access to results about any one person which will help to protect your privacy.

What if I have more questions?

If you have any questions, please talk to your doctor or nurse, or call our research review board at 888-657-3711.