RTOG FOUNDATION

RTOG 3505

(ClinicalTrials.gov NCT #: 02768558*)*

RANDOMIZED, DOUBLE BLINDED PHASE III TRIAL OF CISPLATIN AND ETOPOSIDE PLUS THORACIC RADIATION THERAPY FOLLOWED BY NIVOLUMAB/PLACEBO FOR LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER

Amendment 2: January 30, 2017

RTOG Foundation 3505

TITLE: RANDOMIZED, DOUBLE BLINDED PHASE III TRIAL OF CISPLATIN AND ETOPOSIDE PLUS THORACIC RADIATION THERAPY FOLLOWED BY NIVOLUMAB/PLACEBO FOR LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER

SHORT TITLE: Testing the addition of the immune activating drug, nivolumab, after chemoradiotherapy for lung cancer.

PROTOCOL NO.: RTOG 3505
WIRB® Protocol #20160677

SPONSOR: RTOG Foundation Collaboration with Bristol-Myers Squibb

INVESTIGATOR: Name
Address
City, State Zip
Country

STUDY-RELATED PHONE NUMBER(S): Name
Number (24-hour number required)

The purpose of this consent form is to help you decide if you want to be in the research study. Before any study-related procedures are performed, you will be asked to read and sign this consent form if you wish to participate.

If you have any questions or do not understand something in this form, you should ask the study doctor or study staff. You should also discuss your participation with anyone you choose in order to better understand this study and your options. You should not join this research study until all of your questions are answered.

What is the usual approach to my lung cancer?

You are being asked to take part in this study because you have locally advanced non-small cell lung cancer. People who are not in a study are usually treated with chemotherapy and radiation therapy. There are several FDA-approved chemotherapy drugs that are commonly used along with the radiation therapy, such as cisplatin and etoposide. For patients who receive the usual approach for this cancer, about 15 out of 100 are free of cancer at five years.

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 receive care that is intended to maintain your comfort and dignity.

Why is this study being done?

We will test whether or not receiving nivolumab after the usual chemotherapy (cisplatin and etoposide) with radiation will improve survival for patients with non-small cell lung cancer. Nivolumab can help the immune system recognize cancer cells. Nivolumab following chemotherapy and radiation is not part of the usual treatment for lung cancer. Nivolumab is already FDA-approved for treating patients with metastatic (stage 4) lung cancer, but is investigational, (not approved) for locally advanced (stage 3) lung cancer.

In this study, half of the patients will receive nivolumab and the other half will receive placebo. The placebo will look the same as nivolumab, but it is a non-active substance and will have no effect on your cancer. This study will allow the researchers to know whether the addition of nivolumab is better, the same, or worse than the usual chemotherapy and radiation. If better, the new approach should improve survival compared to the usual approach.

There will be about 660 people taking part in this study.

What are the study groups?

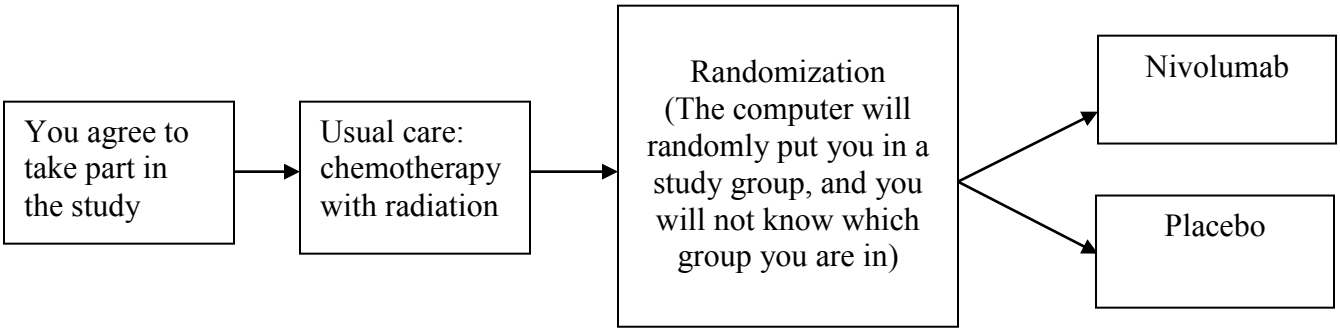
All patients will receive cisplatin and etoposide chemotherapy with radiation. After completion of chemoradiotherapy, eligible patients will be randomized to be in one of two groups (nivolumab or placebo). A computer will by chance assign you to treatment groups in the study. This is called randomization. This is done by chance because no one knows if one study group is better or worse than the other. You will have an equal chance of being placed in either group.

You and your doctors will not know if you are assigned to the nivolumab or placebo group. This is called being "masked." Masking assures that the researchers are able to compare the experience of patients in each group without bias or a preference for one treatment over the other. In the event of an emergency, the study doctor can find out what you are receiving.

After completion of chemoradiotherapy:

- **Nivolumab Group 1** will get nivolumab 240 mg every 2 weeks for 16 weeks, then 480 mg every 4 weeks for 36 weeks for a total of one year.
- **Placebo Group 2** will get placebo every 2 weeks 16 weeks, then every 4 weeks for 36 weeks for a total of for one year.

Another way to find out what will happen to you during this study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.



How long will I be in this study?

You will receive chemotherapy and radiation for 6 weeks. After completion of chemoradiotherapy and if your cancer has not progressed, you will receive nivolumab or placebo every 2 weeks for 16 weeks and then every 4 weeks for 36 weeks for a total of one year. After you finish nivolumab or placebo, you will be seen regularly by your doctors. During these visits, they will check the status of your cancer and your side effects from treatment. These visits will occur every 3 months from the end of treatment for years 1 and 2, every 6 months for years 3, 4, and 5, then once a year for your lifetime.

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 tests and procedures that you will need to have if you take part in this study.

Before you begin the study, you will need to have the following extra tests:

- You must have the tumor tissue from your previous biopsy tested for PD-L1, an immune system marker, using a test that is for research purposes only as the test has not been approved by the FDA for your type of cancer. The role of PD-L1 in cancer is not fully understood and researchers want to use the information from this investigational test of your tumor tissue to help them understand the immune system's response to cancer. The result of the PD-L1 test does not impact the treatment you will receive for your cancer. Your privacy is very important and the researchers will make every effort to protect it. 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. If any of your tissue is left over from this extra test, it will be stored for biobanking, if you agree. There is more information about biobanking in the optional study section.
- You will need to have blood tests to screen for health problems that might increase the side effects of treatment. This would include tests for liver problems, an under- or over-active thyroid, and inflammation of the pancreas. These blood tests will be repeated during treatment to monitor for side effects of nivolumab.
- You will be asked to fill out 3 forms with questions about your physical and emotional well-being. Researchers will use this information to learn more about how cancer and cancer treatment affects people. Each form will take about 5 to 10 minutes to complete. The forms will ask about things like

tiredness and social and emotional well-being. You may feel uncomfortable answering some of the questions, and you can skip any you do not want to answer.

- You will be asked to fill out the three forms 8 times: before chemotherapy and radiation treatment, before nivolumab/placebo treatment, at 3, 6, 9,12, 15 and 18 months from start of nivolumab/placebo treatment. For one of the forms, you will be asked to fill it out 4 more times at years 2, 3, 4, and 5 from start of nivolumab/placebo treatment Each form will take about 5 to 10 minutes to complete. The forms will ask about things like tiredness and social and emotional well-being. You may feel uncomfortable answering some of the questions, and you can skip any you do not want to answer.

During the study:

- You will need to have blood tests to monitor your liver and thyroid function, and to monitor for inflammation of the pancreas.
- Women who can have children must have a negative pregnancy test every 4 weeks in order to continue to take part in the study.
- You will be asked to fill out the same 3 forms with questions about your physical and emotional well-being before nivolumab/placebo treatment, at 3, 6, 9,12, 15 and 18 months from start of nivolumab/placebo treatment. For one of the forms, you will be asked to fill it out 4 more times at years 2, 3, 4, and 5 from start of nivolumab/placebo treatment. Each form will take about 5 to 10 minutes to complete. The forms will ask about things like tiredness and social and emotional well-being. You may feel uncomfortable answering some of the questions, and you can skip any you do not want to answer.

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:

- The study drug(s)/study approach may not be better, and could possibly be worse, than the usual approach for your cancer.
- You may lose time at work or home and spend more time in the hospital or doctor's office than usual
- You may be asked sensitive or private questions which you normally do not discuss

There is also a risk that you could have side effects from the study drug(s)/study approach.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

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

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

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 cisplatin, etoposide, and radiation to the lung which are the usual approach for this type of cancer:

Possible Side Effects of Cisplatin, Etoposide

COMMON, SOME MAY BE SERIOUS In 100 people receiving Cisplatin, Etoposide, more than 20 and up to 100 may have:
• Infection, especially when white blood cell count is low • Anemia which may require blood transfusions • Bruising, bleeding • Kidney damage which may cause swelling, may require dialysis • Hearing loss including ringing in ears • Hair loss • Sores in mouth which may cause difficulty swallowing • Diarrhea, loss of appetite, nausea, vomiting • Tiredness • Fever, chills

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Cisplatin, Etoposide, from 4 to 20 may have:
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Confusion • Difficulty with balance • Heart failure or heart attack which may cause chest pain, shortness of breath, swelling of ankles, and tiredness • Severe skin rash with blisters and peeling which can involve inside of mouth and other parts of the body • Liver damage which may cause yellowing of eyes and skin, swelling

RARE, AND SERIOUS In 100 people receiving Cisplatin, Etoposide, 3 or fewer may have:
• Cancer of bone marrow (leukemia) caused by chemotherapy later in life • Seizure

Possible Side Effects of Lung Radiation

COMMON, SOME MAY BE SERIOUS In 100 people receiving lung radiation, more than 20 and up to 100 may have:
• Swelling and redness, tanning, thickening, numbness, or peeling of the skin in the area of radiation • Difficulty and/or pain with swallowing • Hair loss in the treatment area, may be permanent • Shortness of breath • Cough with or without increased phlegm production

COMMON, SOME MAY BE SERIOUS

In 100 people receiving lung radiation, more than 20 and up to 100 may have:

- Tiredness
- Diarrhea, nausea
- Anemia, which may require blood transfusion
- Infection, especially when white blood cell count is low
- Bleeding, bruising
- Rib pain, increased risk of rib fracture

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving lung radiation, from 4 to 20 may have:

- Inflammation of the lung that may cause difficulty breathing and can be life-threatening
- Narrowing of the throat which may cause vomiting, difficulty swallowing
- Scarring in the lung
- Lung collapse
- Fluid around lungs
- Bleeding from the lungs which may cause coughing up blood
- Fever
- Narrowing of the esophagus which may cause difficulty swallowing
- Pain in chest wall

RARE, AND SERIOUS

In 100 people receiving lung radiation, 3 or fewer may have:

- Abnormal opening in internal organs which may cause pain and bleeding
- Irritation of the heart causing heart failure, heart attack, chest pain, abnormal heartbeat, shortness of breath, swelling of ankles, cough or tiredness
- Transverse myelitis – irritation of the spinal cord causing weakness, tingling or numbness of the lower body and legs, or paralysis of the lower half of the body
- Brachial plexopathy – irritation of the nerves controlling the arm, causing weakness or paralysis
- Bleeding from the airway (windpipe)
- Narrowing of the airway causing shortness of breath
- Death
- Lung damage, may be life threatening
- Damage to the large blood vessels surrounding the heart, which could cause coughing up of blood and possibly death
- Sores and skin damage causing bleeding and severe pain and may lead to an open wound

The risks below are those known to occur with the drug, nivolumab, when given alone. It is unknown if giving nivolumab after chemotherapy and radiation will result in more severe or new side effects or if side effects will worsen more rapidly than expected. Therefore, it is important to promptly notify your study doctor of any side effects even if they are mild.

Possible Side Effects of Nivolumab

Nivolumab may cause one or more of the side effects listed below. This information is based on data from cancer subjects in other clinical trials with nivolumab. In addition, there may be side effects that are not yet

known that may occur. You should tell your doctor or nurse right away about any possible side effects you experience.

PLEASE NOTE THE FOLLOWING IN REVIEWING THESE RISKS:
Nivolumab increases the immune system response and may result in severe and possibly fatal immune-related side effects. Immune-related side effects have been reported in patients receiving nivolumab. Most immune-related side effects are reversible and managed with treatment. It is important to promptly notify your study doctor if you experience any side effects even if they are mild. You will receive a Subject Alert Card with the contact details of your study doctor.

Special precautions Side effects of nivolumab may happen anytime during treatment or even after your treatment has ended. **Call or see your healthcare provider right away if you develop any problems listed below or the symptoms get worse.**
COMMON, SOME MAY BE SERIOUS In 100 people receiving nivolumab, more than 20 and up to 100 may have:
• Tiredness

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Nivolumab, from 4 to 20 may have:
• Anemia which may require blood transfusion • Swelling and redness of the eye • Pain in belly • Diarrhea, nausea, loss of appetite • Dry mouth • Fever • Swelling and redness at the site of the medication injection • Bruising, bleeding • Pain or swelling of the joints • Reaction during or following a drug infusion which may cause fever, chills, rash Nivolumab may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to: • Lung problems (pneumonitis and pleural effusion). Symptoms may include: new or worsening cough, chest pain, shortness of breath. • Intestinal problems (colitis) that can rarely lead to tears or holes in your intestine. Signs and symptoms of colitis may include: diarrhea or increase in bowel movements, blood in your stools or dark, tarry, sticky stools, severe belly pain or tenderness. • Skin: itching; rash, blisters including inside the mouth; loss of skin pigment • Liver problems (hepatitis) which can cause liver failure. Signs and symptoms of hepatitis may include: yellowing of your skin or the whites of your eyes, severe nausea or vomiting; drowsiness; pain in the right upper belly. • Hormone gland problems (especially the thyroid, pituitary and adrenal glands, and

pancreas). Signs and symptoms may include: headaches that will not go away or unusual headaches, extreme tiredness or changes in mood or behavior decreased sex drive; weight loss or weight gain; excessive thirst or urine; dizziness or fainting.

RARE, AND SERIOUS

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

- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat

Nivolumab may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Visual disturbances which may cause double vision, blurred vision, or loss of vision with a chance of blindness
- A condition with high blood sugar which leads to tiredness, frequent urination, excessive thirst, headache, nausea and vomiting, and can result in coma
- Kidney problems, including nephritis and kidney failure requiring dialysis. Signs of kidney problems may include: decrease in the amount of urine, blood in your urine, ankle swelling.
- Heart problems including inflammation and heart failure. Symptoms and signs of heart problem may include: Shortness of breath, swelling of the ankle and body.
- Problem of the muscle, including inflammation, which can cause muscle pain and severe muscle weakness sometimes with dark urine
- Inflammation of the brain (meningitis/encephalitis), which may cause: headache, confusion, sleepiness, seizures, and stiff neck
- Problem of the nerves that can cause paralysis. Signs and symptoms may include: numbness, tingling of hands and feet; weakness of the arms, legs and facial muscle movement.
- Complications associated with stem cell transplant using donor stem cells (allogeneic stem cell transplant). These complications are caused by attack of donor cells on the host organs (inducing liver, skin and gut), and can lead to death. If you are considering an allogeneic stem transplant after participating in this study, please tell your doctor that you have received nivolumab therapy, since the risk and severity of transplant-associated complications may be increased.

Lung Inflammation (pneumonitis): Inflammation of the lung is a rare side effect of nivolumab. Lung inflammation may occur without symptoms but may be seen on x-ray or CT scan. In some cases, lung inflammation may lead to symptoms that may be mild to severe. In rare cases, death has occurred as a result of lung inflammation. Signs and symptoms of lung inflammation may include difficulty breathing, pain or discomfort while breathing, chest pain, cough, shortness of breath, increased rate of breathing, fever, low blood oxygen levels, or fatigue.

Your study doctor and nurse will watch you closely for changes in your ability to breathe and for other signs or symptoms that might show you are developing this type of lung inflammation. If needed, additional tests or procedures may be required to assess your lungs.

Please inform your study doctor or nurse AT ONCE if you experience any of the following:

- Any new or increased shortness of breath;
- Any new or increased chest pain;
- Any new or increased pain/difficulty while breathing;
- Any new or increased cough or any significant change in your type of cough; for example any new or increased mucous or blood in your cough;
- Any change in the amount of oxygen you require;
- Any fever, fatigue, or other symptoms that occur at the same time as any changes to your breathing or other lung symptoms.

Damage to the body by the immune system caused by nivolumab may also include:

Intestinal problems (colitis) that can lead to tears or holes in your intestine. Signs and symptoms of colitis may include**:**

- diarrhea (loose stools) or more bowel movements than usual
- blood in your stools or dark, tarry, sticky stools
- severe stomach area (abdomen) pain or tenderness

Liver problems (hepatitis). Signs and symptoms of hepatitis may include:

- yellowing of your skin or the whites of your eyes
- severe nausea or vomiting

Kidney problems, including nephritis and kidney failure. Signs of kidney problems may include:

- decrease in the amount of urine
- blood in your urine
- swelling in your ankles
- loss of appetite

Hormone gland problems (especially the thyroid and pituitary glands). Signs and symptoms that your hormone glands are not working properly may include:

- headaches that will not go away or unusual headaches
- extreme tiredness, changes in mood, or behavior decreased sex drive,
- dizziness or fainting

Other Problems:

- rash
- changes in eyesight
- severe or persistent muscle pain, weakness or joint pains

Getting medical treatment right away may keep these problems from becoming more serious.

There may be risks or side effects which are unknown at this time.

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

Certain drugs may increase the severity of these side effects if taken during the study. Ask your study doctor for a full list of prohibited medications.

Risks to Reproduction, Unborn Babies and Nursing Infants
You must use an adequate method to avoid pregnancy for the duration of this study and after the last dose of study drug. Women who are able to become pregnant must not be pregnant or breastfeeding and should not become pregnant or breastfeed while taking the study treatments and for up to 5 months after the last dose of study drug. Male subjects who are sexually active with a woman of child bearing potential should also use an adequate method of birth control to avoid pregnancy of their partner for up to 7 months after the last dose of study drug. You should immediately contact your study doctor if there is a change in your method to avoid pregnancy, if you start any prescription drug or other medication (including over-the-counter drugs and herbal supplements) not prescribed by the study doctor, or if you become pregnant, suspect pregnancy or if you missed your period or it is late, or if you have a change in your usual menstrual cycle (e.g., heavier bleeding during your period or bleeding between periods). There may be unknown risks to you, your unborn baby or nursing infant if you are or become pregnant during this study or are breastfeeding during this study.

If you are a woman of childbearing potential, you will have a pregnancy test at the start of treatment with chemotherapy and radiation and again prior to start of treatment with nivolumab/placebo, then every 4 weeks during treatment and during your first two follow up visits. Pregnancy will be determined on basis of either a urine or blood test.

Should you become pregnant during this study, you will immediately have the study medication permanently discontinued and be referred for obstetric care; unless, after further discussion between your physician and the Sponsor of this research, it is decided that the benefit of continuing therapy would outweigh the risk for stopping therapy. You will continue to be followed for any side effects or potential benefits of the study treatment, provided it is safe for you and your unborn baby to do so. Your doctor will discuss this with you, as well as options for additional appropriate care for your cancer. The sponsor has not set aside any funds to pay for any aspects of obstetric, child or related care and does not plan to pay for them.

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.

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

It is not possible to know at this time if the study drug(s)/study approach is better than the usual approach so this study may or may not help you. This study will help researchers learn things that will help 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 or loss of benefits to you. You will not lose medical care or any legal rights.

What are the costs of taking part in this study?

Nivolumab will be supplied by Bristol-Myers Squibb at no charge while you take part in this study. The cost of getting nivolumab ready and giving it to you is not paid by the study sponsor so you or your insurance company may have to pay for this. It is possible that nivolumab may not continue to be supplied 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 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 provided 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 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.

If you are injured as a result of this study, you do not give up your right to pursue a claim through the legal system. The study sponsor agrees to pay for the reasonable cost of necessary medical treatment for any physical injury or illness that is a direct result of receiving study drug, provided that the study plan was followed, and your insurance does not cover the injury services. A study-related injury does not include injuries directly caused by any of the following: any standard of care medical treatments; the natural course of your disease or medical condition; or if you or the study staff did not follow the study plan.

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:

- The study sponsor, RTOG Foundation
- The drug company supporting the study, Bristol-Meyers Squibb (its current or future research partners, collaborators, assignees, licensees or designees and their affiliates, agents, and employees)
- 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 Food and Drug Administration 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 the study [insert name of study doctor] at [insert telephone number].

For questions about your rights while in this study, or if you have concerns or complaint about the research, contact the Western Institutional Review Board (WIRB®) at 1019 39th Avenue SE Suite 120, Puyallup Washington 98374-2115, Telephone: 1-800-562-4789 or 360-252-2500, E-mail: Help@wirb.com.

WIRB is a group of people who perform independent review of research. WIRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WIRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

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 Sample Collections for Laboratory Studies and Biobanking for Possible Future Studies

Researchers are trying to learn more about cancer 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 in this study, the study doctor for the main study would like to collect blood and tumor tissue for research on genetic markers of response to the immunotherapy, including activation of the immune system. If you choose to take part, blood will be drawn and a sample of tissue from your previous biopsy will be collected. Also, if your tumor progresses and you undergo a biopsy, tissue will be collected.

In addition, 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 and supported by the RTOG Foundation.

WHAT IS INVOLVED?

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

1) Over five time-points, a total of 10 tablespoons of blood will be collected from a vein in your arm: before treatment, after chemotherapy and radiation, before nivolumab or placebo, 60 days after start of nivolumab/placebo, and at the time of progression or severe side effects. In addition, a sample from the tissue that was collected at the time of your biopsy will be sent to the Biobank.
2) Your sample and some related health information will be sent to a researcher for use in the study described above. Remaining samples may be stored in the Biobank, along with samples from other people who take part. The samples will be kept until they are used up.
3) For future unspecified research:Your tumor tissue sample 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 RTOG-Foundation 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) The most common risks related to drawing blood from your arm are brief pain and possibly a bruise.
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 can 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 research study. Even though your genes are unique, you share some of the same genes with your blood relatives. Although we are not able to know all of the risks from taking part in research on inherited traits, we believe that the risks to you and your family are very low, because your samples will be coded. Research results will not be returned to you or your doctor.

Very rarely health or genetic information could be misused by employers, insurance companies, and others. For example, life insurance companies may charge a higher rate based on this information.

Many states have laws to protect against genetic discrimination. Additionally, a federal law called the Genetic Information Non-Discrimination Act, or GINA, is in effect. This law prohibits health insurer or employer discrimination (if the employer has 15 or more employees). The law does not include other types of misuse by life insurance, disability, or long term care insurance. To learn more about the GINA Law, please ask the study team.

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 RTOG Foundation staff with access to the list must sign an agreement to keep your identity confidential.
3) Researchers to whom RTOG Foundation 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. The researchers, using the samples from you and others, might make discoveries that could help people in the future.

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, [*insert name of study doctor*] at [*insert telephone number*], who will let the researchers know. Then, any sample that remains in the bank will no longer be used and related health information will no longer be collectd. 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, [*insert name of study doctor*] at [*insert telephone number*], at _____ *(insert telephone number of study doctor for main trial)*.

Please circle your answer to show whether or not you would like to take part in each option (*include only applicable questions)*:

SAMPLES FOR THE LABORATORY STUDIES:

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

YES NO

SAMPLES FOR FUTURE RESEARCH STUDIES:

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

YES NO

I agree that my study doctor, or their representative, may contact me or my physician to see if I wish to participate in other research in the future.

YES NO

This is the end of the section about optional studies.

My Signature Agreeing to Take Part in the Main Study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed copy of this form. I agree to take part in the main study *and any additional studies where I circled 'yes'.*

Participant's signature_____

Date of signature_____

Signature of person(s) conducting the informed consent discussion_____

Date of signature_____