RTOG FOUNDATION

RTOG 3504

(ClinicalTrials.gov NCT #: 02764593)

SAFETY EVALUATIONS OF NIVOLUMAB (ANTI-PD-1) ADDED TO CHEMORADIOTHERAPY (CRT) PLATFORMS IN PATIENTS WITH INTERMEDIATE AND HIGH-RISK LOCAL-REGIONALLY ADVANCED HEAD AND NECK SQUAMOUS CELL CARCINOMA

INFORMED CONSENT

Version January 23, 2018

for

Amendment 4: December 26, 2017

To be attached to protocol version: December 26, 2017

RESEARCH SUBJECT INFORMATION AND CONSENT FORM
RTOG 3504

TITLE:	SAFETY EVALUATIONS OF NIVOLUMAB (ANTI-PD-1) ADDED TO CHEMORADIOTHERAPY (CRT) PLATFORMS IN PATIENTS WITH INTERMEDIATE AND HIGH-RISK LOCAL-REGIONALLY ADVANCED HEAD AND NECK SQUAMOUS CELL CARCINOMA
PROTOCOL NO.:	RTOG 3504 WIRB® Protocol #20160353
SPONSOR:	RTOG Foundation Collaboration with Bristol-Myers Squibb
INVESTIGATOR:	Name Address City, State Zip Country
STUDY-RELATED PHONE NUMBER(S):	Name Number(s) (24-hour number required)

Study Title for Study Participants: Testing the safety of adding an immune system activator, nivolumab, to two types of chemoradiotherapy in advanced head and neck cancer

Official Study TITLE for Internet Search on http://www.ClinicalTrials.gov: Safety Evaluations of Nivolumab (Anti-PD-1) Added to Chemoradiotherapy (CRT) Platforms in Patients with Intermediate and High-Risk Local-Regionally Advanced Head and Neck Squamous Cell Carcinoma

What is the usual approach to my head and neck cancer?

You are being asked to take part in this study because you have advanced head and neck cancer of the oropharynx, oral cavity, larynx, or hypopharynx. People who are not in a study are usually treated with a combination of radiation therapy, surgery, and/or chemotherapy. There are several chemotherapy drugs that are commonly used together with radiation therapy. These include cisplatin and cetuximab. Approximately 6 out of every 10 patients who receive the usual therapy for head and neck cancer are free of cancer five years after completing treatment.

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
- you may choose not to be treated for cancer. If you decide that you don't want active treatment, one of your options is called "comfort care." Comfort care includes pain medication and other support. It aims to maintain your comfort and dignity rather than cure disease. Usually this care can be provided at home.

  If you think you might prefer comfort care, please discuss this with your family, friends and your doctor.

Why is this study being done?

The researchers will test the safety of adding nivolumab to radiation therapy and to the most common combinations of radiation therapy and chemotherapy. Nivolumab can help the immune system recognize cancer cells. Nivolumab is already FDA-approved for treating patients with lung cancer and melanoma (a type of skin cancer). However, nivolumab is not part of the usual treatment of advanced head and neck cancer and is investigational in this study. The addition of nivolumab to radiation or to radiation given with chemotherapy may or may not help shrink your cancer or prevent it from coming back. Nivolumab may or may not increase the side effects of radiation therapy and chemotherapy. In this study, the researchers will carefully evaluate the side effects patients experience when nivolumab is added to standard treatment.

There will be about 40 people taking part in this study.

What are the study groups?

There are four study groups. All patients will receive nivolumab plus one of three usual treatments. The usual treatments include radiation with cisplatin (Groups 1 and 2), radiation with cetuximab (Group 3), or radiation alone (Group 4) for patients who cannot tolerate chemotherapy. Nivolumab will be given at a dose that is recommended when giving nivolumab treatment alone or in combination with chemotherapy.

<u>Patients who can tolerate chemotherapy</u>

The first patients who enter the study that can tolerate chemotherapy will be assigned to Group 1 until enrollment is complete. The next patients who enter the study will be assigned to group 2 until enrollment is complete followed by group 3.

<u>Patients who cannot tolerate chemotherapy</u>

Any patient who enters the study who cannot tolerate chemotherapy will be assigned to Group 4.

You will know which of the following groups you are assigned to:

Group 1 (weekly cisplatin): All patients will receive nivolumab in combination with radiation therapy and cisplatin. The first dose of nivolumab will be given 14 days prior to starting radiation therapy and cisplatin. Nivolumab will be given every 2 weeks for a total of ten doses. Cisplatin will be given every week of radiation therapy for a total of 7 doses.

Group 2 (every 3-week cisplatin): All patients will receive nivolumab in combination with radiation therapy and cisplatin. The first dose of nivolumab will be given 14 days prior to starting radiation therapy and cisplatin. Starting on the first day of radiation, nivolumab will be given every 3 weeks for a total of six doses. Cisplatin will be given every 3 weeks for a total of 3 doses during radiation treatment.

Group 3 (cetuximab): All patients will receive nivolumab in combination with radiation therapy and cetuximab. The first dose of nivolumab will be given 14 days prior to starting radiation therapy. Nivolumab will be given every 2 weeks for a total of ten doses. The first dose of cetuximab will be given 7 days prior to starting radiation therapy. Cetuximab will be given every week of radiation therapy for a total of 8 doses.

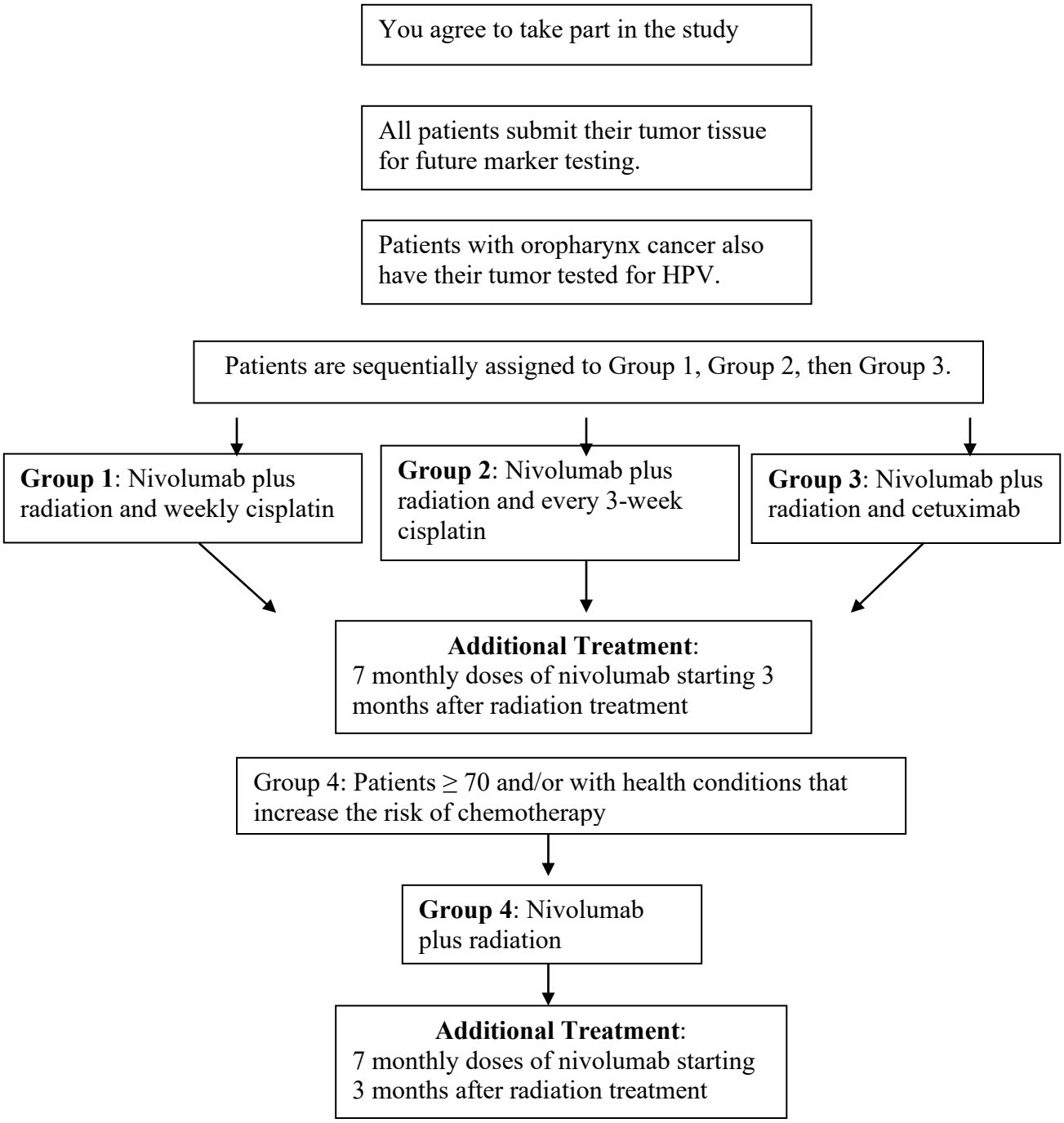
Some people have health conditions that increase the risk of chemotherapy. These include poor kidney function, nerve damage, hearing loss, or low energy. It may also be difficult for some people over the age of 70 to tolerate chemotherapy. If you are older than 70 or have one of these health conditions, you may still participate in this study. Your doctor may decide that radiation alone is the preferable treatment. Therefore, in Group 4, nivolumab will be given with radiation therapy alone.

Group 4 (radiation alone), for p16-negative or HPV-related oropharynx cancer patients and for oral cavity, larynx and hypopharynx cancer patients aged 70 years and older and/or with health conditions that increase the risk of chemotherapy. All patients will receive nivolumab in combination with radiation therapy. The first dose of nivolumab will be given 14 days prior to starting radiation therapy. Nivolumab will be given every 2 weeks for a total of 10 doses.

Additional treatment: Patients in all groups will be eligible to receive 7 monthly doses of nivolumab starting 3 months after completing radiation treatment, so the side effects of continuing nivolumab therapy for a total of one year of treatment can be tested.

Nivolumab, cisplatin, and cetuximab are intravenous ("IV") medications. This means they are given as an infusion into a vein through an "IV."

Another way to find out what will happen to you during this study is to read the chart below. Start reading at the top and read down, following the arrows.



How long will I be in this study?

Patients in all groups will receive radiation therapy and nivolumab with or without chemotherapy for approximately 16 weeks. All patients will then be eligible to receive additional nivolumab therapy for a total of one year. After you finish radiation treatment, 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 two weeks after the last dose of nivolumab, and every 3 months from the end of radiation treatment for two years.

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 to find out if you can be in the study:

1. You must submit your tumor tissue from your previous biopsy to be 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.
2. Patients with oropharynx cancer must have their tumor tissue tested for the Human Papillomavirus (HPV). Oropharynx cancers that are positive for p16 expression are considered to be HPV-related and usually have a better response to treatment. Your test results will be available to your doctor. 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.
3. You will be asked for information about your lifetime history of smoking cigarettes.
4. 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 hepatitis, an underactive thyroid, and inflammation of the pancreas. These blood tests will be repeated during treatment to monitor for side effects of nivolumab. State law requires that the results of positive tests for hepatitis be reported to a local health agency.

During the study:

1. You will need to have blood tests to monitor your endocrine function (your body's ability to produce hormones needed to make many of your body's organs work) and to monitor your liver function.

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 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.

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.

The risks below are those known to occur with the drugs when they are given alone. It is unknown if the combination of either cisplatin or cetuximab with nivolumab 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 inflammation may occur and symptoms may be mild to severe. In rare cases, death has occurred as a result of lung inflammation. Signs and symptoms of lung inflammation include difficulty breathing, pain or discomfort while breathing, chest pain, cough, shortness of breath, increased rate of breathing, fever, 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 <u>AT ONCE</u> 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.

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.

Possible Side Effects of Cisplatin

COMMON, SOME MAY BE SERIOUS In 100 people receiving Cisplatin, more than 20 and up to 100 may have:
• Nausea, vomiting • Infection, especially when white blood cell count is low • Anemia, which may cause tiredness, or may require blood transfusions • Bruising, bleeding • Kidney damage, which may cause swelling, may require dialysis • Hearing decrease, including ringing in ears

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Cisplatin, from 4 to 20 may have:
• Hair loss • Change in taste • Diarrhea • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Confusion • Difficulty with balance • Numbness and tingling of the arms and legs • Blurred vision or changes in ability to see colors (especially blue or yellow)

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

Possible Side Effects of Cetuximab

COMMON, SOME MAY BE SERIOUS In 100 people receiving Cetuximab, more than 20 and up to 100 may have:
• Change in nails • Swelling and redness of the area of radiation • Rash, itching, dry skin, acne • Dehydration, weight loss, loss of appetite • Sores in mouth which may cause difficulty swallowing • Constipation, diarrhea, vomiting, nausea • Difficulty sleeping • Headache, tiredness • Pain • Fever • Infection, especially when white blood cell count is low • Cough, shortness of breath

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Cetuximab, 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, depression, worry • Fainting • Severe blood infection • Blood clot which may cause swelling, pain, shortness of breath

RARE, AND SERIOUS In 100 people receiving Cetuximab, 3 or fewer may have:
• Scarring of the lungs • Kidney damage which may require dialysis • Heart stops beating

Possible Side Effects of Radiation Therapy to the Head and Neck

COMMON, SOME MAY BE SERIOUS In 100 people receiving head and neck radiation therapy, more than 20 and up to 100 may have:
• Sores in the mouth and throat which may be painful especially with swallowing • Dry mouth, changes in taste, reduced sense of smell—some level of change likely to be permanent • Thick saliva • Hoarseness • Skin changes such as swelling and redness of the skin in the area of radiation • Pain or pressure in the ear • Tiredness • Weight loss • Hair loss in the area or radiation (face, chin, neck) • Cavities, tooth decay; loss of teeth; tooth sensitivity

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving head and neck radiation therapy, from 4 to 20 may have:
• Decrease in function of the thyroid gland that may require you to take thyroid replacement medicine • Damage to the nerves of the shoulder and arm which may cause decreased movement and feeling • Ear infection • Hearing loss • Difficulty swallowing which may require a long term or permanent feeding tube

RARE, AND SERIOUS In 100 people receiving head and neck radiation therapy, 3 or fewer may have:
• Breathing and swallowing problems that may require a surgical procedure to create an opening through the neck into the windpipe • Damage to the nerves in the head and neck that control sensation, expression, or other motor functions • Damage to the jawbone which may cause jaw pain and loosening of teeth • Damage to the voice box or nerves to the voice box which may cause hoarseness, shortness of breath, inability to speak • Damage to the skin, soft tissues, or other parts of the head and neck that may require a major operation to correct and, rarely, can be life threatening

Risks to Reproduction, Unborn Babies and Nursing Infants

You must not be pregnant or breastfeeding, and you should not become pregnant or breastfeed while you are taking the study treatments. Females should not breastfeed while receiving nivolumab and up to 18 weeks from the last dose of nivolumab. You must use an adequate method to avoid pregnancy for the duration of this study and for up to 23 weeks 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 31 weeks 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 or if you start any prescription drug or other medication (including over-the-counter drugs and herbal supplements) not prescribed by the study doctor. 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.

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?

The treatment with the experimental agent being given with standard therapy is unlikely to help you more than the standard therapy alone. 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 to you or loss of benefits. You will not lose medical care or any legal rights.

For questions about your rights while in this study, or if you have questions, concerns, or complaints about the research, you may contact: Western Institutional Review Board at 1019 39th Avenue SE Suite 120, Puyallup Washington 98374-2115, 1-800-562-4789 or 360-252-2500, or email 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.

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 the 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 the 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 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 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 RTOG Foundation.
- Bristol-Myers Squibb.
- 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 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 website 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, complaints, or concerns you have about this study or to report side effects or injuries. Contact the study *doctor* [insert name of study doctor[s]] *at* [insert telephone number].

ADDITIONAL STUDIES SECTION: This section is about optional studies you can choose to take part in

This part of the consent form is about an optional study that you can choose to take part in. You will not get health benefits from this study. 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 this optional study. You can still take part in the main study even if you say 'no' to this study. If you sign up for but cannot complete the study for any reason, you can still take part in the main study.

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

To be attached to protocol version: December 26, 2017

Optional Sample Collections for Laboratory Studies and Biobanking for Possible Future Studies

Researchers are trying to learn more about cancer. 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 the optional laboratory study, the study doctor for the main study would like to collect blood for research on markers of response to the immunotherapy, including activation of the immune system (antibodies and lymphocytes).

If you choose to take part in the optional biobanking, the researchers ask your permission to store leftover blood from the laboratory study and leftover tissue from your previous biopsy, 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 and supported by the RTOG Foundation.

WHAT IS INVOLVED?

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

1) For the laboratory study: About 10 tablespoons of blood will be collected from a vein in your arm before treatment, and at 3 and 6 months after treatment.
2) For future unspecified research: Your leftover blood sample, leftover 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.
3) 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.
4) 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.
5) 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.

   Some states have laws to protect against genetic discrimination. A federal law called the Genetic Information Non-Discrimination Act, or GINA is in effect. This law does not allow discrimination by insurers or employers. 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 [Name] at [Phone Number].

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 samples are 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 the 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. Your samples may be helpful to research whether you do or do not have cancer. The researchers, using the samples from you and others, might make discoveries that could help people in the future.

To be attached to protocol version: December 26, 2017

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 for main trial]* at *[insert telephone number of study doctor for main trial]* 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 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, _____*[insert name of study doctor for main trial]*, 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 STUDY:

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.

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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 name_____

Participant's signature _____

Date of signature _____

Name of person(s) conducting the informed consent discussion _____

Signature of person(s) conducting the informed consent discussion _____

Date of signature _____