SWOG CANCER RESEARCH NETWORK

Version Date: August 10th, 2023

TO: ALL NATIONAL CLINICAL TRIALS NETWORK (NCTN) PARTICIPANTS; CTSU

FROM: SWOG Operations Office (E-Mail: protocols@swog.org)

RE: **S2107,** "Randomized Phase II Trial of Encorafenib and Cetuximab with or without Nivolumab (NSC #748726) for Patients with Previously Treated, Microsatellite Stable, BRAFV600E Metastatic and/or Unresectable Colorectal Cancer"

REVISION #3

Study Chair: Van Morris, M.D.
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Action Codes
(√) Expedited review allowed
(√) Patients Must be Informed*
(√) Consent Must Be Amended*

* See "Patient Notification and Use of Consent Addendum" and "Regulatory Considerations" instructions below.

Key Updates
(√) Other: CAEPR Update for nivolumab (NSC 748726)
(√) Informed Consent Changes
(√) Patient notification required

Sites using the CIRB as their IRB of record: The protocol and/or informed consent form changes have been approved by the CIRB and must be activated within 30 days of distribution of this notice through the CTSU Bi-Monthly Broadcast email.

REVISION #3

The above referenced study has been revised with the following changes in response to the Rapid Request for Amendment (RRA) for nivolumab (NSC 748726) received on August 3, 2023, from Howard Streicher, M.D. (streicherh@ctep.nci.nih.gov), Jeffrey Moscow, M.D. (jeffrey.moscow@nih.gov), and Meg Mooney, M.D. (mooneym@ctep.nci.nih.gov). The associated action letter is attached.

Protocol Changes

1. The version date has been updated.
2. Throughout the protocol, formatting, typographical errors, pagination, and cross-references have been corrected as needed.
3. The table of contents has been updated
4. Section 3.3, Nivolumab (BMS-936558, MDX1106, Opdivo®) (NSC # 748726) (IND-[redacted]):

   The CAEPR has been updated to Version 2.5, June 10, 2023.

   - **Added New Risk:**
     - **Rare but Serious: Blood and lymphatic system disorders - Other (lymphatic dysfunction)**

- **Clarifications to Existing Risks**
  - Hepatobiliary disorders – Other immune-mediated hepatitis: Updated *immune-mediated* to *immune-related*.
  - Immune system disorders - Other (sarcoidosis): Updated to include *sarcoid granuloma*.
  - Renal and urinary disorders - Other (immune-mediated nephritis): Updated *immune-mediated* to *immune-related*.
  - Respiratory, thoracic and mediastinal disorders - Other (bronchiolitis obliterans with organizing pneumonia): Updated to include acronym *BOOP*.
  - footnote 3 was added to Eye disorders - Other (Vogt-Koyanagi-Harada)

Model Consent Form Changes

1. The version date has been updated.

2. "Drug Risks": The following changes have been made to the nivolumab risks section:

   - The Table of Possible Side Effects for nivolumab version date has been updated.
   - **Added New Risk:**
     - **Rare and serious: Swelling of arms and legs which may cause a feeling of heaviness and tightness**

Patient Notification and use of Consent Addendum:

SWOG has determined that the changes above that are bolded may affect a patient's willingness to participate in the study; therefore, SWOG requires that patients be notified of these changes.

Who must be informed?

- All patients currently on study treatment with nivolumab or who may receive treatment with nivolumab on the study in the future.

How must patients be notified?

- For patients currently receiving nivolumab or who may receive treatment with nivolumab on the study in the future: Notification must take place either via the attached Consent Addendum or via amended consent form by next study visit. After the change has been discussed with the patient, the patient must sign and date either the Consent Addendum or the 08/10/2023 version of the consent form.

What is the notification deadline and process?

- For patients currently receiving treatment with nivolumab who may receive treatment with nivolumab on the study in the future: Patients must be notified by their next scheduled visit or within 90 days after CTSU distribution of this revision, whichever is sooner.
- CIRB has approved the attached Consent Addendum; therefore, the Consent Addendum may be utilized immediately to notify patients of these changes.

Regulatory Considerations:

Do local consent forms need to be updated?
- Yes, local consent forms must be updated to include all the changes in this revision.

Can accrual continue until local implementation of the 08/10/2023 version of the consent form?

Unless otherwise noted in the Action Letter, accrual may continue; however:

- Patients enrolled after the notification deadline must be enrolled under the 08/10/2023 version of the consent form.
- Patients enrolled prior to the notification deadline but before the 08/10/2023 version is implemented locally may be consented by signing the previous version of the consent form 05/31/2023 together with signing the attached Consent Addendum.

- **PLEASE NOTE: If the Action Letter requires suspension of accrual until the updated consent is implemented locally, the Action Letter instructions supersede this memo.**

The updated protocol, model informed consent form, case report forms, and patient-reported outcome forms can be accessed from the CTSU website (www.ctsu.org). Please discard any previous versions of the documents and replace them with the updated versions. Please contact giquestion@crab.org or 206/652-2267 with any questions.

This memorandum serves to notify the NCI, and SWOG Statistics and Data Management Center.

cc: PROTOCOL & INFORMATION OFFICE
Ian (Zishuo) Hu, MD, PhD – Alliance Champion
Rimini Breakstone, MD – NRG Champion
Thomas B. Karasic, MD -- ECOG-ACRIN Champion

Informed Consent Addendum Model for S2107

S2107 "Randomized Phase II Trial of Encorafenib and Cetuximab with or without Nivolumab (NSC #748726) for Patients with Previously Treated, Microsatellite Stable, BRAF*V600E* Metastatic and/or Unresectable Colorectal Cancer"

The following information should be read as an update to the original Consent form that you read and signed at the beginning of the study. Unless specifically stated below, all information contained in that original Consent Form is still true and remains in effect. Your participation continues to be voluntary. You may refuse to participate, or may withdraw your consent to participate at any time, and for any reason, without jeopardizing your future care at this institution or your relationship with your study doctor.

New or additional information

The following new risk has been identified as a rare, but serious risk:

Swelling of arms and legs which may cause a feeling of heaviness and tightness

Patient Signature and Date

By signing this form, I acknowledge that I have read the information above or had it read to me. I have discussed it with a member of the study team and my questions have been answered. I understand that I will be given a copy of this form.

Participant's signature (or legally authorized representative)_____

Date of signature_____

Signature of person(s) conducting the informed consent discussion_____

Date of signature_____

Research Study Informed Consent Document

Study Title for Participants: Testing the addition of Nivolumab to standard treatment for patients with metastatic colorectal cancer that have a BRAF mutation

Official Study Title for Internet Search on http://www.ClinicalTrials.gov:
Protocol S2107, "Randomized Phase II trial of encorafenib and cetuximab with or without nivolumab (NSC #748726) for patients with previously treated, microsatellite stable, BRAFV600E metastatic and/or unresectable colorectal cancer," (NCT #05308446)

Overview and Key Information

What am I being asked to do?

We are asking you to take part in a research study. This study has public funding from the National Cancer Institute (NCI), part of the National Institutes of Health (NIH) in the United States Department of Health and Human Services. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer.

We are asking you to take part in this research study because you have colorectal cancer that has spread, and the cancer has a change in the gene called the $BRAF^{V600E}$ gene.

Taking part in this study is your choice.

You can choose to take part, or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered. See the "Where can I get more information?" section for resources for more clinical trials and general cancer information.

Why is this study being done?

This study is being done to answer the following question:

Can we lower the chance of colorectal cancer growing or spreading by adding a drug to the usual combination of drugs?

We are doing this study because we want to find out if this approach is better or worse than the usual approach for your colorectal cancer. The usual approach is defined as care most people get for colorectal cancer.

What is the usual approach to my colorectal cancer?

The usual approach for patients who are not in a study is treatment with the combination of encorafenib and cetuximab, which has been approved by the Food and Drug Administration (FDA).

What are my choices if I decide not to take part in this study?

- You may choose to have the usual approach described above.
- You may choose to take part in a different research study if one is available.
- You may choose not to be treated for cancer.
- You may choose to only get comfort care to help relieve your symptoms and not get treated for cancer.

What will happen if I decide to take part in this study?

If you decide to take part in this study, you will either get encorafenib, cetuximab, and nivolumab or you will get encorafenib and cetuximab until the treatment stops working, your side effects become too great, you choose to stop participating, whichever comes first.

After you finish the study treatment, your doctor will continue to follow your condition for 3 years and watch you for side effects. During this time, you will have clinic visits or phone calls every 6 months. You will also have a CT or MRI scan approximately every 8 weeks until your disease gets worse. Scans will continue under the care of your doctor during the duration of your routine visits.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks

We want to make sure you know about a few key risks right now. We give you more information in the “What risks can I expect from taking part in this study?” section.

If you choose to take part in this study, there is a risk that the study treatment may not be as good as the usual treatment at stopping the cancer from growing.

There is also a risk that you could have side effects from the combination of nivolumab and the standard treatment. These side effects may be worse and may be different than you would get with the usual approach for colorectal cancer.

Some of the most common side effects that the study doctors know about are:

- Fatigue/lack of energy
- Skin rash
- Nausea/vomiting
- Headache

There may be some risks that the study doctors do not yet know about.

Benefits

It is not possible to know now if nivolumab will delay tumor growth compared to the usual approach. This study will help the study doctors learn things that will help people in the future.

If I decide to take part in this study, can I stop later?

Yes, you can decide to stop taking part in the study at any time.

If you decide to stop, let your study doctor know as soon as possible. It's important that you stop safely. This may mean slowly stopping the study drugs so that there is not a sudden unsafe change, causing risk to your health. If you stop, you can decide if you want to keep letting the study doctor know how you are doing.

Your 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.

Are there other reasons why I might stop being in the study?

Yes. The study doctor may take you off the study if:

- Your health changes and the study is no longer in your best interest.
- New information becomes available, and the study is no longer in your best interest.
- You do not follow the study rules.
- For women: You become pregnant while on the study.
- The study is stopped by the Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsor (the National Cancer Institute [NCI]). The study sponsor is the organization who oversees the study.

It is important that you understand the information in the informed consent before making your decision. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask your study doctor or nurse.

What is the purpose of this study?

The purpose of this study is to compare the usual treatment alone to using nivolumab plus the usual treatment. The addition of nivolumab to the usual treatment could stop the cancer from growing or spreading. But it could also cause side effects, which are described in the risks section below.

This study will help the study doctors find out if this different approach is better than the usual approach. To decide if it is better, the study doctors will be looking to see if the nivolumab will delay tumor growth in patients by 3 months or more compared to the usual approach.

There will be about 84 people taking part in this study.

What are the study groups?

This study has 2 study groups.

- **Group 1**

  If you are in this group, you will get encorafenib (as pills) once daily, cetuximab every 2 weeks through a vein, and nivolumab every 28 days through a vein.

  You also will keep a pill diary. This helps you keep track of when you take your pills. The study doctor will show you how to use this diary. Each time you visit the clinic, you must bring the pill diary, any remaining pills, and the pill bottle.

  There will be about 56 people in this group.

- **Group 2**

  If you are in this group, you will get encorafenib (as pills) once daily and cetuximab every 2 weeks through a vein.

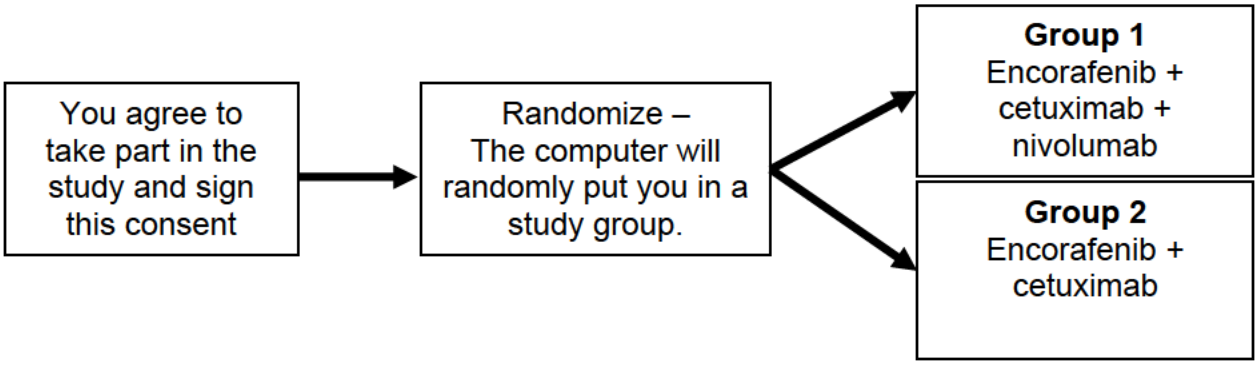
  You also will keep a pill diary. This helps you keep track of when you take your pills. The study doctor will show you how to use this diary. Each time you visit the clinic, you must bring the pill diary, any remaining pills, and the pill bottle.

  There will be about 28 people in this group.

If the disease gets worse during your care, you and your study doctor will determine whether you want to stay on this study and continue receiving study treatment, or whether you want to stop receiving study treatment. If the disease appears to be getting worse or the tumors appear to be getting larger, you may still be able to receive the study drugs if you and your doctor decide it is in your best interest. This is because sometimes the disease appears to get worse, but the study drug is actually working. However, there are risks of continuing to receive the study drug. For example, the disease may be getting worse and may reach the point that you are no longer able to receive other treatments. You are still at risk for side effects due to the study drug. This could also delay starting other treatments. If you choose to receive the study drug after the disease appears to get worse, you will continue to have study visits as described in the main consent. The study doctor will discuss this option with you. Other options for treatment after growth of your cancer would need to be discussed with your doctor and could include more chemotherapy or a different clinical trial.

We will use a computer to assign you to one of the study groups. This process is called "randomization." It means that your doctor will not choose, and you cannot choose which study group you are in. You will be put into a group by chance. You will have a two to one chance of being in Group 1 or Group 2, respectively.

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.



What exams, tests, and procedures are involved in this study?

Before you begin the study, your doctor will review the results of your exams, tests, and procedures. This helps your doctor decide if it is safe for you to take part in the study. If you join the study, you will have more exams, tests, and procedures to closely monitor your safety and health. Most of these are included in the usual care you would get even if you were not in a study.

Listed below are exams, tests, and procedures that need to be done as part of this study to monitor your safety and health but may not be included in the usual care. We will use them to carefully follow the effects of the study treatment, including preventing and managing side effects.

These exams, tests, and procedures to monitor your safety and health include:

- Blood counts done every two weeks during treatment.
- EKG prior to beginning treatment

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

General Risks

If you choose to take part in this study, there is a risk the addition of Nivolumab may not be as good as the standard treatment alone at shrinking your cancer.

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.

The nivolumab and standard therapy used in this study could be very harmful to an unborn or newborn baby. There may be some risks that doctors do not yet know about. It is very important that you check with your study doctor about what types of birth control or pregnancy prevention to use during the study and for 5 months after you have completed the study.

Side Effect Risks

The addition of nivolumab 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 test your blood and let you know if changes occur that may affect your health.

There is also a risk that you could have other 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 your study doctor. He or she can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.
- Your study doctor may adjust the study drugs to try to reduce side effects.

This study is looking at a combination of the usual drugs used to treat this type of cancer plus a study drug. This different combination of drugs may increase your side effects or may cause new side effects.

Drug Risks

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

Group 1 & 2
Possible Side Effects for Encorafenib

COMMON, SOME MAY BE SERIOUS In 100 people receiving encorafenib, more than 20 and up to 100 may have:
• Dry skin • Feeling tired • Hair loss • Itching • Muscle pain or joint pain • Nausea • Reddening, swelling, numbness and peeling on palms and soles (hand foot skin reaction) • Skin rash including redness, itching, hives and raised areas of skin • Thickening of external part of the skin • Tingling, numbness or abnormal sensitivity to pain or touch and nerve pain • Alteration of the light sensing part of the back of the eye that may affect your vision • Increase in a lab test result for creatine phosphokinase (an enzyme found in the blood) that may indicate muscle inflammation or damage.

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving encorafenib, from 10 to 20 may have:

- Decreased appetite
- Difficulty sleeping
- Increase in blood test results that check how well the liver is working
- Pain including pain in the arms and legs and back pain
- Skin tags, new moles on the skin or changes in existing moles
- Small, rough bumps on the skin
- Vomiting
- Weakness
- Swelling of or damage to the light sensing part of the eye or impaired vision

OCCASIONAL, SOME MAY BE SERIOUS
In 100 people receiving encorafenib, from 1 to 10 may have:

- Abdominal pain
- Change in how food tastes or change in ability to taste
- Constipation
- Feeling that you are dizzily turning around
- Fever
- High blood sugar
- Inflammation of the eye causing eye discomfort, redness and sensitivity to light
- Increase in a blood test result that checks how well your kidneys are working
- Low red blood cell count
- Muscle weakness and spasms
- New skin growths, including skin cancer
- Weakness of facial muscles or loss of facial movement
- Decrease in a test of the heart's ability to pump blood (decreased ejection fraction or left ventricular dysfunction)
- Dizziness
- High blood pressure
- Inflammation in the intestine that may cause pain, spasms, diarrhea or bleeding
- Reduction in the kidney's ability to filter wastes

RARE, AND SERIOUS
In 100 people receiving encorafenib, 1 or fewer may have:

- Inflammation (swelling) of the pancreas causing pain in the stomach that may also be felt in the back and may be associated with nausea or vomiting. The symptoms can be mild and may go away without treatment, but in some cases can be more severe, needing treatment.
- In addition, there may be a rare side effect of changes in the electrical activity of your heart called QT prolongation. QT prolongation can cause irregular heartbeats that can be life-threatening. Associated symptoms might include shortness of breath, fast or slow heartbeat and lightheadedness or fainting.
- Bleeding in the stomach, intestines, or rectum
- Blood clots in the lungs

PLEASE NOTE THE FOLLOWING IN REVIEWING THESE RISKS:

BMS-936558 is an agent involved in the inhibition of "immune checkpoints," and may result in severe and possibly fatal immune-mediated side effects probably due to activation and growth of immune cells (T-cells). Immune-mediated side effects have been reported in patients receiving BMS-936558. In clinical trials, most immune-mediated side effects were reversible and managed by stopping BMS-936558 temporarily, administration of corticosteroids and supportive care.

Group 1 Only

Possible Side Effects of Nivolumab
(Table Version Date: June 10, 2023)

Special precautions
Side effects of Nivolumab may happen anytime during treatment or even after your treatment has ended. Some of these problems may happen more often when Nivolumab is used in combination with ipilimumab. **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
- Diarrhea, nausea
- Dry mouth
- Fever
- Swelling and redness at the site of the medication injection
- Bruising, bleeding
- Pain or swelling of the joints
- Loss of appetite
- Reaction during or following a drug infusion which may cause fever, chills, rash

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

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

RARE, AND SERIOUS

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

- Swelling of arms and legs which may cause a feeling of heaviness and tightness
- Dry eyes
- Sores in the mouth which may cause difficulty swallowing
- A syndrome starting with flu-like symptoms and followed by swelling, tenderness which may cause flu-like symptoms, blurred vision, ringing in the ears, changes in hair or hair loss
- Swelling of the bowels

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

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

Group 1 & 2

Possible Side Effects of Cetuximab
(Table Version Date: August 5, 2020)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Cetuximab, more than 20 and up to 100 may have:
• Shortness of breath, cough • Infection, especially when white blood cell count is low • Diarrhea, constipation, nausea, vomiting, weight loss, dehydration • Sores in mouth • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Numbness and tingling of the arms and legs • Headache, tiredness, fever • Difficulty sleeping • Swelling and redness of the area of radiation • Rash, itching, dry skin, peeling skin, acne • Change in nails • Pain

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Cetuximab, from 4 to 20 may have:
• Damage to the heart • Blood clot in lung which may cause swelling, pain, shortness of breath • Swelling and redness of the whites of the eye • Swelling and redness at the site of medication injection • Heartburn • Dry mouth, changes in taste • Confusion, worry, depression • Chills • Severe skin rash with blisters and can involve inside of mouth and other parts of the body • Nail infection • Hair loss

RARE, AND SERIOUS In 100 people receiving Cetuximab, 3 or fewer may have:
• Heart attack which may cause chest pain, shortness of breath, or sudden death • Scarring of the lungs • Severe blood infection • Kidney damage which may require dialysis

Additional Drug Risks

The study drug could interact with other drugs and food. Participants must avoid consumption of grapefruit, pomegranates, star fruits, Seville oranges or products containing the juice of each during the entire study and preferably 7 days before the first dose of study drugs, due to potential interaction with the study drugs. Orange juice is allowed.

The study drug could interact with other drugs. You will be given a study specific wallet card that lists these possible interactions. Share this information with your family members, caregivers, other health providers, and pharmacists.

Rarely, there are problems getting enough supplies of the study drug. If that happens, your doctor will talk with you about your options.

What are my responsibilities in this study?

If you choose to take part in this study, you will need to:

- Keep your study appointments.
- Tell your doctor about:
    - all medications and supplements you are taking
    - any side effects
    - any doctors' visits or hospital stays outside of this study
    - if you have been or are currently in another research study.
- Write down in your medication diary when you take the study drug at home.

For women: Do not get pregnant or breastfeed while taking part in this study.

For men: Do not father a baby while taking part in this study.

For all: Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 5 months after your last dose of study drug.

What are the costs of taking part in this study?

You and/or your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your cancer.

This includes:

- the costs of tests, exams, procedures, and drugs that you get during the study to monitor your safety and prevent and treat side effects.
- the costs of getting the nivolumab ready and giving it to you.
- your insurance co-pays and deductibles.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it doesn't pay for if you take part in this clinical trial. Also, find out if you need approval from your plan before you can take part in the study.

Ask your doctor or nurse for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

You or your insurance provider will not have to pay for the nivolumab while you take part in this study.

Taking part in this study may mean that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat the type of cancer you have. You may:

- Have more travel costs.
- Need to take more time off work.
- Have other additional personal costs.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

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

If you are injured as a result of taking part in this study and need medical treatment, please talk with your study doctor right away about your treatment options. The study sponsors will not pay for medical treatment for injury. Your insurance company may not be willing to pay for a study-related injury. Ask them if they will pay. If you do not have insurance, then you would need to pay for these medical costs.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. Agreeing to take part in this study does not mean you give up these rights.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at or receive copies of some of the information in your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.

Some of these organizations are:

- The study sponsor, SWOG Cancer Research Network, and any company supporting the study now or in the future. This would include any organization helping the company with the study.
- The NCI Central IRB, which is a group of people who review the research with the goal of protecting the people who take part in the study.
- The FDA and the groups it works with to review research.
- The NCI and the groups it works with to review research.
- The NCI's National Clinical Trials Network and the groups it works with to conduct research

In addition to storing data in the study database, data from studies that are publicly funded may also be shared broadly for future research with protections for your privacy. The goal of this data sharing is to make more research possible that may improve people's health. Your study records may be stored and shared for future use in public databases. However, your name and other personal information will not be used.

Some types of future research may include looking at your information and information from other patients to see who had side effects across many studies or comparing new study data with older study data. However, right now we don't know what research may be done in the future using your information. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your information.

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.

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 doctor (*insert name of study doctor[s]*) at (*insert telephone number, and email address if appropriate*).

For questions about your rights while in this study, call the (*insert name of organization or center*) Institutional Review Board at (*insert telephone number*).

Optional studies that 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. They are separate from the main study described above. These optional studies will not benefit your health. The researchers leading these optional studies 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.

Taking part in these optional studies is your choice. You can still take part in the main study even if you say "no" to any or all of these studies. There is no penalty for saying "no." You and your insurance company will not be billed for these optional studies. If you sign up for, but cannot complete any of these 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 known laboratory studies and/or storage for possible future studies

Researchers are trying to learn more about cancer and other health problems using blood and tissue samples from people who take part in clinical trials. By studying these samples, researchers hope to find new ways to prevent, detect, treat, or cure diseases.

Some of these studies may be about how genes affect health and disease. Other studies may look at how genes affect a person's response to treatment. Genes carry information about traits that are found in you and your family. Examples of traits are the color of your eyes, having curly or straight hair, and certain health conditions that are passed down in families. Some of the studies may lead to new products, such as drugs or tests for diseases.

Unknown future studies

If you choose to take part in this optional study, tissue and blood samples will be collected and stored. Storing samples for future studies is called "biobanking." The biobank is being run by SWOG Biobank and is supported by the NCI. This is a publicly funded study. Samples from publicly funded studies are required to be shared as broadly as possible. However, we will protect your privacy. The goal of this is to make more research possible that may improve people's health.

The biobank is a public research resource. It has controlled access. This means that researchers who want to get samples and data from it must submit a specific research request. The request identifies who they are and what their planned research project is. Before getting the samples and data, the researchers must agree to keep the data private, only use it for their planned research project, and never use it to try to identify you.

Right now, we don't know what research may be done in the future using your blood and tissue samples. This means that:

- You will not be asked if you agree to take part in the future research studies.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your samples.

Unknown future research studies may include sequencing of all or part of your DNA. This is called genomic sequencing. Sequencing allows researchers to identify your genetic code. Changes in your genetic code may just be in your tumor tissue. These are called somatic changes. Changes may also be in your normal tissue and passed down through your family. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down. These are called germline changes. If only tumor tissue is sequenced, we will not know if a genetic change in your tumor is also in your normal tissue. This is why sometimes both normal tissue and tumor tissue are sequenced. This helps researchers understand if a genetic change happened only in the cancer tissue, or in your normal tissue as well.

This part of the consent form is about optional studies that you can choose to take part in. They are separate from the main study described above. These optional studies will not benefit your health. The researchers leading these optional studies hope the results will help other people with cancer in the future. The results will be added to your medical records and you or your study doctor will know the results.

Taking part in these optional studies is your choice. You can still take part in the main study even if you say "no" to any or all of these studies. There is no penalty for saying "no." You and your insurance company will not be billed for these optional studies. If you sign up for but cannot complete any of these studies for any reason, you can still take part in the main study.
You will be asked to circle your choice of "yes" or "no" for the optional studies at the end of the consent form.

What is involved in this optional sample collection?

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

1. About 2 ½ tablespoons of blood will be collected at 4 time points from a vein in your arm: At your 1st study visit, at your 3rd or 4th study visit, at your 9th study visit and after you come off treatment. A sample from the tissue that was collected at the time of your surgery will be sent to the biobank. Also, the tissue sent to the expert pathologist (described above) will be stored in the biobank.
2. Your samples will be stored in the biobank. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until they are used for research or destroyed.
3. Researchers can only get samples from the biobank after their research has been approved by experts. Researchers will not be given your name or contact information.
4. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

What are the risks in this optional sample collection?

- The most common risks related to drawing blood from your arm are brief pain and maybe a bruise.
- Generally, hospitals will keep some of your tissue. This tissue may be used to help treat you for cancer in the future. There is a small risk that when this tissue sample is submitted to the biobank for this optional sample collection, your tissue could be used up.
- Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find 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 and get or keep health insurance. There are laws against the misuse of genetic information, but they may not give full protection. For more information about the laws that protect you, ask your study doctor or visit: https://www.genome.gov/10002328/.

How will information about me be kept private?

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

1. They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information.

2. Researchers who study your sample and information will not know who you are. They also must agree that they will not try to find out who you are.
3. Your personal information will not be given to anyone unless it is required by law.
4. If research results are published, your name and other personal information will not be used.

What are the benefits to taking part in this optional sample collection?

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 to this optional sample collection?

There are no costs to you or your insurance. You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What if I change my mind about this optional sample collection?

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 biobank know. Then, any sample that remains in the biobank will be destroyed or returned to your study doctor. This will not apply to any samples or related health information that have already been given to or used by researchers.

What if I have questions about this optional sample collection?

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 below to show if you would or would not like to take part in each optional study:

Samples for unknown future studies:

I agree that my samples and related health information may be kept in a biobank for use in future health research.

YES NO

Contact for future research

I agree that my study doctor, or someone on the study team, may contact me or my doctor 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 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 and dated copy of this form. I agree to take part in the main study. I also agree to take part in any additional studies where I circled "yes".

Participant's signature (or legally authorized representative)

_____

Date of signature_____

Signature of person(s) conducting the informed consent discussion

_____

Date of signature _____