ECOG-ACRIN
cancer research group
Reshaping the future of patient care

April 21, 2025

Martha Kruhm, MS RAC
Head, Protocol and Information Office
Quality Assurance Section
CTEP, DCT, NCI
6130 Executive Blvd, EPN Room 7000
Bethesda, MD 20892

Dear Ms. Kruhm:

Enclosed is Addendum #9 to EA6194, *Phase II Randomized Study of Neoadjuvant Pembrolizumab Alone or in Combination with CMP-001 in Patients with Operable Melanoma: Efficacy and Biomarker Study.*

There are no revisions to the case report forms as a result of this amendment.

Please replace your current copy of the protocol and Informed Consent document with these updated versions. We recommend that each institution maintain a file containing the original protocol, Informed Consent, and all subsequent revisions/versions.

IRB Review Requirements:

This addendum has been reviewed and approved by the Central IRB, which is the sole IRB of record for this study. The protocol and/or informed consent form changes must be activated within 30 days of the CIRB posting of this notice.

EA6194, *Phase II Randomized Study of Neoadjuvant Pembrolizumab Alone or in Combination with CMP-001 in Patients with Operable Melanoma: Efficacy and Biomarker Study* dated April 9th, 2025. The CIRB stipulation include changes in response to a Pembrolizumab (MK-3475, NSC 776864) rapid request for amendment from Dr. Brian Ko dated April 11, 2025. Please note that the Principal Investigator's comments appear in bold below.

I. Changes made in response to the CIRB stipulations: Protocol

#	Section	Comments
1.	5.5.1	Add modification in response to Pembrolizumab RRA CAEPR Version 2.9, January 31, 2025. **PI Response: This has been resolved.**

II. Changes made in response to the CIRB stipulations: Consent

#	Section	Comments
2.	Possible Side Effects of Pembrolizumab (MK-3475)	Add modifications in response to Pembrolizumab RRA CAEPR Version 2.9, January 31, 2025 **PI Response: This has been resolved.**

28 State Street, Suite 1100, Boston, MA 02109 p: 857.504.2900 f: 617. 589.0914 ecog-acrin.org

III. Additional changes: Protocol

#	Section	Comments
3.	3.1.9	Removed “sexual orientation or” per CTEP request.
4.	5.4	Updated the adverse event reporting requirements per the Global Safety Update.
5.	5.5.2	Updated the note for CMP-001 (NSC 820014).

The following revisions to EA6194 protocol have been made in this addendum:

	Section	Change
1.	Global	Updated version date throughout. Removed “gender” and replaced with “sex” throughout.
2.	Cover Page	Added Ahmad Tarhini, M.D., Ph.D as the Translational Sciences Co-Chair. Added Addendum #9.
3.	Table of Contents	Added Appendix VIII “CIMAC Correlative Biomarker Study”
4.	Appendix VIII	Added the CIMAC Correlative Biomarker Study language.

The following revisions to EA6194 Informed Consent Document have been made in this addendum:

	Section	Change
1.	Global	Updated version date throughout.

If you have any questions regarding this addendum, please contact Amelia Thornton at athornton@ecog-acrin.org or 857-504-2900.

We request review and approval of this addendum to EA6194 so ECOG-ACRIN may activate it promptly.

Thank you.

Sincerely,

Pamela Cogliano

Senior Director, Protocol Development

Research Study Informed Consent Document

Study Title for Participants: A study evaluating whether Pembrolizumab alone or in combination with CMP-001 improves efficacy in patients with operable melanoma.

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Protocol EA6194, Phase II Randomized Study of Neoadjuvant Pembrolizumab Alone or in Combination with CMP-001 in Patients with Operable Melanoma: Efficacy and Biomarker Study.

Version Date: April 21, 2025

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 advanced melanoma that is still considered resectable by surgery. In this study, "advanced melanoma" is defined as melanoma spread to the skin or lymph nodes at regional or distant sites from the original site of the primary melanoma.

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:

Will treatment before surgery with either pembrolizumab alone, or pembrolizumab combined with CMP-001, cause your melanoma to shrink enough that no more living tumor cells are evident at the time of surgery. This study will also try to answer whether these forms of immunotherapy can affect the chances of the melanoma returning ("relapse risk") and the chances of death from melanoma ("survival").

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

What is the usual approach to stage III B/C/D resectable melanoma?

The usual approach for patients who are not in a study is treatment with surgery followed by a type of immunotherapy that belongs to a class of drugs called PD-1 inhibitors (two drugs pembrolizumab and nivolumab are approved by the FDA for this indication) or a type of drugs called targeted therapy if your melanoma has a mutation called BRAF (two drugs given in combination called dabrafenib and trametinib are approved by the FDA for this indication).

Your doctor will explain which treatment may be best for your melanoma and will talk to you more about these treatments.

Please notice that pembrolizumab is FDA-approved for the treatment of melanoma after a person has undergone surgical resection. It is not approved before surgery. CMP-001 is not FDA-approved for the treatment of any disease.

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 your cancer.

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

If you decide to take part in this study, you will be randomized to receive either pembrolizumab alone (every 3 weeks) for up to 9 weeks, or pembrolizumab (every 3 weeks) in combination with CMP-001 for up to 9 weeks. If your treatment includes CMP-001, it will be injected under the skin at the first week of treatment, then directly into the tumor tissue once a week for 6 additional weeks. Following this pre-operative therapy, you will undergo scans to assess the tumor's response and will then undergo surgery. Surgery is usually done within 2-4 weeks after the scans are completed.

Following recovery from surgery, you will get pembrolizumab alone every 6 weeks for up to 8 treatments.

After you finish your study treatment, your doctor will continue to follow your condition for up to 10 years after you join the study.

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 drugs may not be as good as the usual approach for your cancer at shrinking or stabilizing your cancer. There is also a risk that you could have side effects from the study drug(s). These side effects may be worse and may be different than you would get with the usual approach for cancer.

Some of the most important risks that may result from participating in this study:

- The side effects resulting from the study drugs as summarized later in this consent and divided into "common", "occasional" and "rare" based on their frequency of occurrence.
- Side effects resulting from combining the 2 study drugs that we may not know about at this time.
- Risks and discomfort resulting from the injection of CMP-001 into the melanoma.
- Delay in the surgery for your melanoma or possibly not being able to do the surgery for your melanoma if the melanoma progresses in its current location or in other parts of your body.

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

Benefits

It is not possible to know at this time if the study approach will reduce the risk of cancer returning after surgery compared to the usual approach alone followed by immunotherapy after recovery from surgery. This study will help the study doctors learn if the treatment approach being studied 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, risk to your health, etc. 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 National Cancer Institute (NCI) Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsor. 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 pembrolizumab alone to using CMP-001 plus pembrolizumab in the neo-adjuvant setting. Neo-adjuvant treatment is treatment that is provided before surgery to try to shrink your cancer and reduce the amount of surgery required. Pembrolizumab is approved by the FDA in the adjuvant setting (after surgery) and is being studied in other trials in the neo-adjuvant setting.

The addition of CMP-001 to pembrolizumab could improve the ability of the immune system to shrink your cancer and to prevent it from returning. 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 combination approach is better than pembrolizumab alone. To decide if it is better, the study doctors will assess how either treatment group affects tumor shrinkage and response to immunotherapy, the likelihood of cancer returning ("relapse risk") and the likelihood of death from cancer ("overall survival").

What are the study groups?

After you register in this study, you will be randomized to one of two pre-operative treatment groups. Some participants will not be treated but will undergo screening tests.

This study has 2 study groups. You will be told which group you are in.

- **Group A**

  If you are in this group, you will get pembrolizumab through a peripheral vein (intravenously) every 3 weeks for 3 doses (3 cycles). See the study calendar for more information.

  There will be about 30 people in this group.

- After this, you will undergo scans and surgery.
- Following surgery, you will continue to receive pembrolizumab intravenously every 6 weeks for up to 8 doses.

- **Group B**

  If you are in this group, you will get a study drug called CMP-001 plus pembrolizumab used to treat this type of cancer. You will get pembrolizumab through a peripheral vein (intravenously) every 3 weeks for 3 doses (3 cycles). In addition, you will receive seven doses of CMP-001 given on a weekly basis. The first CMP-001 will be given under the skin (subcutaneously) for one dose only followed by CMP-001 injected into the tumor ("intra-tumoral injection") for the remaining 6 doses of CMP-001. See the study calendar for more information.

Rev. Add3 If you have more than one tumor that can be injected, CMP-001 will ideally be injected into the largest tumor, but it may be injected into another tumor based on accessibility and ease of administration. More than one accessible tumor may be injected if determined to be best course of action in your case by your physician.

  Patients must be observed for at least 4 hours following the first six doses of CMP-001 injection and must be observed for at least 1 hour following the seventh dose of CMP-001 injection.

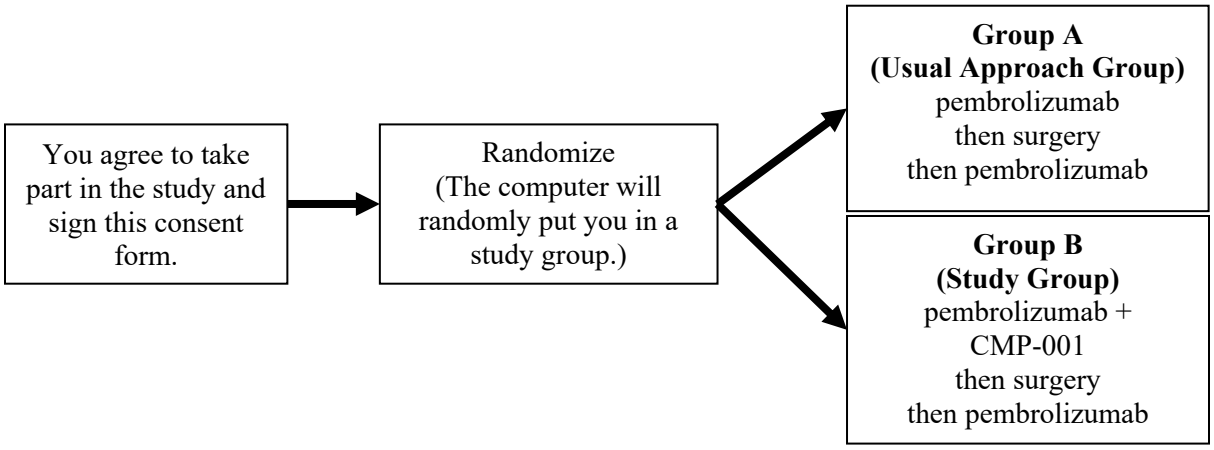
  You will receive up to 7 doses of CMP-001 before surgery. You will not be able to get additional doses of the drug after surgery. This drug is not approved by the FDA for treatment of your disease.

  There will be about 30 people in this group.

  - After this, you will undergo scans and surgery.
  - Following surgery, you will continue to receive pembrolizumab intravenously every 6 weeks for up to 8 doses.

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 an equal (50%) chance of being in Group A or Group B.

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.

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

- Blood counts
- Thyroid testing
- Physical exams
- Submission of your tissue for central review: Small pieces of previously collected tissue from your tumor and from your surgery will be sent to central reviewers to be studied. This review is to determine how your disease responded to treatment and is done for this research study only. The results of the review will not be given to you or your doctor, will not be placed in your medical record and will not affect your medical 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 that the study drug may not be as good as the usual approach for your cancer or condition at stabilizing 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 immunotherapy 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 26 weeks after you have completed the study.

Side Effect Risks

The immunotherapy 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 immunotherapy.

Here are important things to know about side effects:

1. The study doctors do not know who will or will not have side effects.
2. Some side effects may go away soon, some may last a long time, and some may never go away.
3. Some side effects may make it hard for you to have children.

4. 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.

Study Group A and Group B – Possible side effects of pembrolizumab alone or in combination with CMP-001 are listed in the tables below. Most of the side effects with these drugs are related to the activation of your immune system and in the case of CMP-001 may include low blood pressure:

Possible Side Effects of Pembrolizumab (MK-3475)

(CAEPR Version 2.9, January 31, 2025)

COMMON, SOME MAY BE SERIOUS In 100 people receiving pembrolizumab (MK-3475), more than 20 and up to 100 may have:
• Tiredness Pembrolizumab (MK-3475) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to: • Anemia which may require blood transfusion

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving pembrolizumab (MK-3475), from 4 to 20 may have:
• Constipation, nausea • Loss of appetite • Pain in back • Joint stiffness • Cough • Swelling and redness of the skin

OCCASIONAL, SOME MAY BE SERIOUS

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

Pembrolizumab (MK-3475) 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:

- Pain in lymph nodes
- Blood clot which may cause bleeding, confusion, paralysis, seizures and blindness
- Hormone gland problems (especially the thyroid, pituitary and adrenal glands, and pancreas). Signs and symptoms may include: headaches that will not go away or unusual headaches, extreme tiredness or changes in mood or behavior decreased sex drive; weight loss or weight gain; excessive thirst or urine; dizziness or fainting
- Intestinal problems (colitis) that can rarely lead to tears or holes in your intestine. Signs and symptoms of colitis may include: diarrhea or increase in bowel movements, blood in your stools or dark, tarry, sticky stools, severe belly pain or tenderness
- Diarrhea
- Sores in the mouth which may cause difficulty swallowing
- Pain in belly
- Sores in the bowels
- Chills, fever
- Reaction during or following a drug infusion which may cause fever, chills, rash, low blood pressure
- 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
- Lung problems (pneumonitis and other conditions). Symptoms may include: new or worsening cough, chest pain, shortness of breath
- Pain or swelling of the joints
- Problem of the muscle, including swelling, which can cause muscle pain and severe muscle weakness sometimes with dark urine
- Skin: itching; acne; rash (can be severe); blisters and peeling on the skin; skin changes; hives

RARE, AND SERIOUS

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

- 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
- Inability to digest food which may cause bloating
- Swelling of the gallbladder

RARE, AND SERIOUS

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

- Swelling of the spinal cord
- Feeling of "pins and needles" in arms and legs
- Redness, pain or peeling of palms and soles

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

- Heart problems including swelling and heart failure. Symptoms and signs of heart problem may include: Shortness of breath, swelling of the ankle and body
- Swelling and redness of the eye which may cause blurred vision with a chance of blindness
- Swelling of the bowels
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Damage to organs in the body when donor cells attack host organs which may cause yellowing of eyes and skin, itchy dry skin
- Damage to organs in the body when the body produces too many white cells
- A condition with high blood sugar which leads to tiredness, frequent urination, excessive thirst, headache, nausea and vomiting, and can result in coma
- Problem of the nerves that can cause paralysis. Signs and symptoms may include: numbness, tingling of hands and feet; weakness of the arms, legs
- Swelling of the brain (encephalitis/meningitis) which may cause headache, confusion, sleepiness, seizures and stiff neck
- Kidney problems, including nephritis and kidney failure requiring dialysis. Signs of kidney problems may include: decrease in the amount of urine, blood in your urine, ankle swelling
- Skin rash developing 1-8 weeks after a drug is given which may be accompanied by fever, lymph node swelling and organ failure
- Swelling or tenderness of blood vessels

Pembrolizumab works by helping your immune system to fight your cancer. However, pembrolizumab can also cause your immune system to attack normal organs and tissues in your body and can affect the way they work, which can result in side effects. These side effects may be serious (i.e. causing hospitalization or be life threatening), may result in death, and/or may occur after you stop taking pembrolizumab. These side effects can affect more than one of your normal organs and tissues at the same time.

Study Group B - In addition to side effects listed above, people who are in Group B may also have some side effects from CMP-001. These side effects are listed below.

Possible Side Effects of CMP-001

(Table Version Date: Version 2.3, September 23, 2024)

COMMON, SOME MAY BE SERIOUS In 100 people receiving CMP-001, more than 20 and up to 100 may have:
• Nausea, vomiting • Chills, tiredness • Swelling and redness at the site of the medication injection • Headache • Low blood pressure which may cause feeling faint

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving CMP-001, from 4 to 20 may have:
• Anemia which may require blood transfusion • Abnormal heartbeat • Pain including pain in belly, joints, back, muscles • Constipation, diarrhea • Swelling of arms, legs • Fever • Reaction during or following a drug infusion which may cause fever, chills, rash • Infection • Weight loss • Loss of appetite • Dizziness • Difficulty sleeping • Shortness of breath • Increased sweating • Itching, rash • Flushing • High blood pressure which may cause headaches, dizziness, blurred vision

RARE, AND SERIOUS In 100 people receiving CMP-001, 3 or fewer may have:
• Damage to organs (heart, lungs) which may cause shortness of breath

RARE, AND SERIOUS In 100 people receiving CMP-001, 3 or fewer may have:
• Swelling and redness of the eye • Flu-like symptoms including body aches • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat

Additional Drug Risks

Rarely, there are problems getting enough supplies of the study drug. If that happens, your doctor will talk with you about your options. You will be given a study information wallet card. Share this with your family members, caregivers, other healthcare providers, and pharmacists.

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.

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 26 weeks 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 immunotherapy agents 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 pembrolizumab or CMP-001 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 your cancer. 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 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
- The Imaging and Radiation Oncology Core (IROC)

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 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.

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 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.

Taking part in this optional study is your choice. You can still take part in the main study even if you say "no" to this study. There is no penalty for saying "no." You and your insurance company will not be billed for this study. If you sign up for, but cannot complete this study for any reason, you can still take part in the main study.

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

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 sample collections for 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 ECOG-ACRIN 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. Also, any health-related information, such as your response to cancer treatment, results of study tests, and medicines you took, will be stored for future use.

Right now, we don't know what research may be done in the future using your 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.

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 your cancer tissue, or in your normal tissue as well.

What is involved in this optional sample collection?

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

1. Tissue leftover after the central reviews, which are a required part of this trial, will be stored for future research. Additional tissue from these procedures may also be sent to be stored. Only tissue samples from procedures performed as part of your care will be submitted.
2. If you agree that additional samples may be submitted for research about four (4) tablespoons of blood will be collected before you start treatment, before Cycle 2 treatment, before your surgery, during adjuvant treatment after the surgery, and when you complete your adjuvant treatment. Blood will also be collected and sent if your disease becomes worse or if it recurs. The blood will usually be collected at the same time as the blood collected for your clinical tests to monitor your health. In most cases, an additional needle stick will not be required to collect blood.
3. If you agree to allow a biopsy to be done to collect tissue samples for research, additional tumor tissue biopsies will be done before you begin treatment. These tumor tissue collections are optional and not considered part of your standard care and will be performed only if you give your consent below, if the risks from the biopsy are low, and the institution treating you has approved to allow the biopsies to be done. You or your insurance company will not be responsible for these biopsies.
4. Your sample 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.
5. 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.
6. 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. Rarely, an infection can happen where the needle was placed. Feeling dizzy or fainting can also happen, but should only last a few minutes after blood is drawn.

Common risks involved in collecting a new tumor biopsy could include bleeding, pain, and/or infection. Before having this procedure, you will be asked to indicate that you understand the nature of the surgical procedure to be performed, it will be determined that the risks for you are relatively small, and that you give your permission before the procedure.

Generally, hospitals will keep some of your tissue. This tissue may be used to help treat your 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 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 the optional study:

Samples for unknown future studies:

May we have some of your tumor tissue from your original biopsy and surgery for future research?

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

YES NO

May your tissue samples (if your disease becomes worse or recurs) and your blood samples collected while you are in the trial be submitted for future research?

I agree to provide additional samples for research.

YES NO

May biopsies be performed to collect tissue for research studies? These biopsies will be done only if it is considered that the procedure may only have small risks, as described above, and the institution has agreed that the biopsies may be done.

I agree biopsies may be done to obtain research samples.

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 _____

Date of signature _____

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

Date of signature _____