Study Title for Study Participants: A Phase II/III Trial of Nivolumab, Ipilimumab, and GM-CSF in Patients with Advanced Melanoma

Official Study Title for Internet Search on http://www.ClinicalTrials.gov/:

EA6141: Randomized Phase II/III Study of Nivolumab plus Ipilimumab plus Sargramostim versus Nivolumab plus Ipilimumab in Patients with Unresectable Stage III or Stage IV Melanoma

What is the usual approach to my melanoma?

You are being asked to take part in this research study because you have melanoma. People who are not in a research study are usually treated with surgery, chemotherapy, and radiation therapy. There are several FDA-approved chemotherapy drugs that are commonly used along with the radiation therapy. For patients who receive the usual approach for this cancer, about 3 out of 100 are free of cancer at five years.

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

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

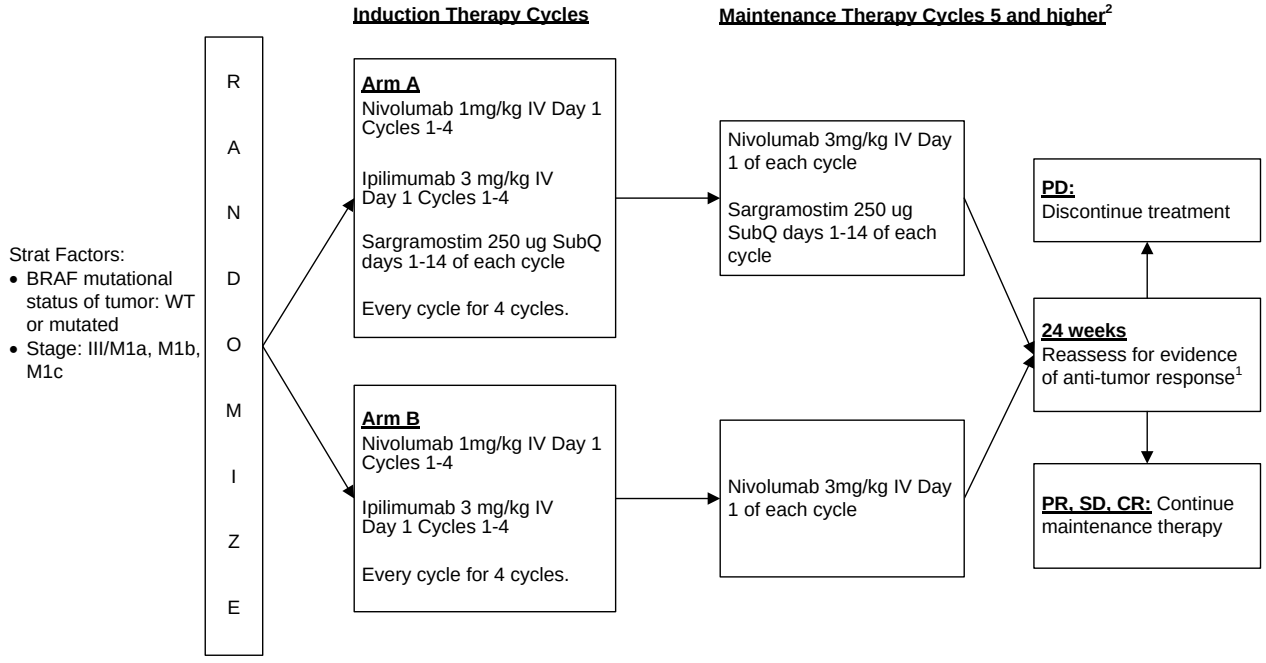
- you may choose to have the usual approach described above
- you may choose to take part in a different research study, if one is available
- or you may choose not to be treated for cancer, but you may want to receive comfort care to relieve symptoms.

Why is this study being done?

The purpose of this research study is to compare any good and bad effects of giving ipilimumab, nivolumab, and GM-CSF (Sargramostim) at the same time compared to just ipilimumab and nivolumab together. We would also like to find out what effects, good and bad, that this combination of drugs may have on your cancer. This study will involve the addition of the FDA approved agent nivolumab to the standard FDA approved ipilimumab immunotherapy in the hopes that it might further improve the good effects of the immunotherapy component of the treatment sequence. The combination of ipilimumab and nivolumab has been shown in recent studies to produce superior antitumor effects but also more side effects than ipilimumab alone. This combination has received FDA approval for

patients with BRAF V600 wild-type unresectable or metastatic melanoma. This combination is under review for FDA approval for patients with BRAF V600 mutant melanoma and is therefore still considered to be experimental for these patients. GM-CSF is a protein that your body normally produces to signal to your body to make white blood cells. White blood cells are very important in the body's defense system as they help identify and destroy foreign invaders, such as bacteria, viruses, and cells that don't belong, such as cancer cells. Injections of GM-CSF increase your body's production of white blood cells and also help enhance the function of the white blood cells. This research study will allow the researchers to know whether this different approach is better, the same, or worse than the usual approach. To be better, the study drugs should improve how long you are able to live with your cancer compared to the usual approach. There will be about 600 people taking part in this research study.

What are the study groups?



1. Scans will be done at week 12 but treatment should continue until week 24 regardless of progression unless treatment is contraindicated by Section 5.6.
2. Patients will receive protocol therapy until progressive disease, non-protocol therapy, or up to two years, whichever comes first.

This research study has two study groups, Arm A and Arm B. Arm A will receive the study drugs nivolumab, ipilimumab, and GM-CSF, followed by just nivolumab and GM-CSF. Arm B will receive nivolumab, and ipilimumab, followed by just nivolumab.

A computer will by chance assign you to treatment groups in the research study. This is called randomization. This is done by chance because no one knows if one study group is better or worse than the other.

If you are in Arm A

Induction Phase: Weeks 1 through 12/Cycles 1-4

If you take part in this research study, you will receive the study drugs ipilimumab and nivolumab at cycles 1, 2, 3, and 4, where each cycle equals 21 days for a total of four infusions. You will have your vital signs measured prior to the infusion. The whole infusion process takes about 3 ½ to 4 hours.

If your doctor has recommended that you take GM-CSF at home, your doctor, nurse, or pharmacist should have instructed you and/or your caregiver on how GM-CSF should be prepared, how it should be injected, and how often it should be injected.

Physical Exams: During all treatment cycles, you will have a physical exam, including measuring your weight. You will be asked questions about your general health and specific questions about any problems that you might be having and any medications you may be taking.

Please tell your doctor about **any** medical treatments that you will have to get during the study (such as elective surgery).

Blood Tests: Every cycle, you will undergo blood tests to closely follow you while you are receiving the study drug. These tests will be done more often than if you were not on this study. Approximately 4-6 tablespoons of blood will be needed at each visit.

Study Diary: You will be asked to record the daily doses of GM-CSF you self inject in a diary. You will also be asked to record any missed or skipped doses. The diary should capture the date, dose, and time of the drug administration, including side effects such as irritation at the injection site or pain and swelling.

Assessment of your cancer: By CT (Computerized Tomography) of your chest, abdomen, and pelvis and an MRI (Magnetic Resonance Imaging) of your brain. These assessments will be performed every 12 weeks.

Maintenance Phase: Weeks 13 and higher/Cycles 5 and higher

If your disease remains stable or continues to improve, you may receive additional doses of nivolumab every 3 weeks after the last dose you received at cycle 4.

During the maintenance phase, you will continue to self inject GM-CSF for the first 14 days of every 21 day cycle.

You could continue the maintenance phase of therapy for up to two years.

Experience with the drug ipilimumab has shown that for some patients, their disease may get larger before it stabilizes or gets smaller. If your disease is getting larger, we may continue to follow and treat your disease at the discretion of you and your doctor.

If you are in Arm B

Induction Phase: Weeks 1 through 12/Cycles 1-4

If you take part in this research study, you will receive the study drugs ipilimumab and nivolumab at cycles 1, 2, 3, and 4, where each cycle equals 21 days for a total of four infusions. You will have your vital signs measured prior to the infusion. The whole infusion process takes about 3 ½ to 4 hours.

Physical Exams: During all treatment cycles, you will have a physical exam, including measuring your weight. You will be asked questions about your general health and specific questions about any problems that you might be having and any medications you may be taking.

Please tell your doctor about **any** medical treatments that you will have to get during the study (such as elective surgery).

Blood Tests: Every cycle you will undergo blood tests to closely follow you while you are receiving the study drug. These tests will be done more often than if you were not on this study. Approximately 4-6 tablespoons of blood will be needed at each visit.

Assessment of your cancer: By CT (Computerized Tomography) of your chest, abdomen, and pelvis and an MRI (Magnetic Resonance Imaging) of your brain. These assessments will be performed every 12 weeks.

Maintenance Phase: Weeks 13 and higher/Cycles 5 and higher

If your disease remains stable or continues to improve, you may receive additional doses of nivolumab every 3 weeks after the last dose you received at cycle 4.

You could continue the maintenance phase of therapy for up to two years.

How long will I be in this study?

During the initial part of the research study (induction), you will be treated for 4 courses, which takes about 3 months. If your cancer is under control after the 4th course, you will continue therapy. After you finish treatment, your doctor will continue to watch you for side effects and follow your condition for 5 years from registration.

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 care for your cancer. However, there are some extra exams and tests that you will need to have if you take part in this research study.

Before you begin the study:

You will need to have the following extra exams and tests to find out if you can be in the research study:

- Blood tests for studies of blood counts.

During the study:

- Blood tests for studies of blood counts, taken every three weeks while receiving study drug.

Central review of your tumor specimen

Small pieces of previously collected tissue from your tumor will be sent to a central laboratory to be reviewed. This review is simply to confirm that you have melanoma.

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

If you choose to take part in this research study, there is a risk that:

- 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
- The study drug(s)/study approach may not be better, and could possibly be worse, than the usual approach for your cancer.
- There can also be a risk in finding out new genetic information about you. New health information about inherited traits that might affect you or your blood relatives could be found during a study.

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

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

Here are important points about side effects:

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

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

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

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

Study Arm A and Arm B – Possible side effects of Ipilimumab:

Possible Side Effects of Ipilimumab

(Table Version Date: March 29, 2019)

Special precautions
Side effects of ipilimumab (MDX-010) may happen anytime during treatment or even after your treatment has ended. Some of these problems may happen more often when ipilimumab (MDX-010) is used in combination with BMS-936558 (nivolumab). **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 ipilimumab (MDX-010), more than 20 and up to 100 may have:
• Diarrhea, nausea • Tiredness Ipilimumab (MDX-010) 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: • Skin: itching; rash, blisters including inside the mouth (can be severe); hives

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving ipilimumab (MDX-010), from 4 to 20 may have:
• Abnormal heartbeat • Hearing loss • Swelling and redness of the eye • Pain

OCCASIONAL, SOME MAY BE SERIOUS
In 100 people receiving ipilimumab (MDX-010), from 4 to 20 may have:

- Difficulty swallowing, eating
- Constipation, vomiting
- Weight loss, loss of appetite
- Fever
- Dehydration
- Pain or swelling of the joints
- Reaction during or following a drug infusion which may cause fever, chills, rash
- Low blood pressure which may cause feeling faint

Ipilimumab (MDX-010) 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). 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
- 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.
- Problem of the muscle, including inflammation, which can cause muscle pain and severe muscle weakness sometimes with dark urine
- 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.
- 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 ipilimumab (MDX-010), 3 or fewer may have:

- Bleeding
- Blockage of the bowels which may cause constipation

RARE, AND SERIOUS In 100 people receiving ipilimumab (MDX-010), 3 or fewer may have:
• Fluid around heart • Severe illness with multiorgan failure • Confusion Ipilimumab (MDX-010) 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: • A condition with high blood sugar which leads to tiredness, frequent urination, excessive thirst, headache, nausea and vomiting, and can result in coma • Heart problems including inflammation and heart failure. Symptoms and signs of heart problem may include: Shortness of breath, swelling of the ankle and body • 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 ipilimumab therapy, since the risk and severity of transplant-associated complications may be increased. • Swelling of the brain (meningitis/encephalitis), which may cause: headache, confusion, sleepiness, seizures, and stiff neck

* This is applicable for patients who have undergone a stem cell transplant.

Possible Side Effects of Nivolumab

(Table Version 2.4, December 2, 2020)

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 urination; dizziness or fainting.

RARE, AND SERIOUS

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

- 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 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, 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.

Possible Side Effects of Sargramostim

(Table Version Date: October 24, 2013)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Sargramostim, more than 20 and up to 100 may have:
• Diarrhea, vomiting • Internal bleeding which may cause black tarry stool, or blood in vomit • Pain • Chills, fever, tiredness • Infection • Weight loss • Itching, rash

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Sargramostim, from 4 to 20 may have:
• Abnormal heartbeat • Bleeding of the eye which may cause blurred vision with a chance of blindness

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Sargramostim, from 4 to 20 may have:
• Difficulty swallowing • Swelling of arms, legs • Bleeding in the brain which may cause headache, confusion • Worry • Kidney damage which may cause swelling, may require dialysis • Fluid in the organs which may cause low blood pressure, shortness of breath, swelling of ankles

RARE, AND SERIOUS In 100 people receiving Sargramostim, 3 or fewer may have:
• None

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

Reproductive risks:

You should not become pregnant or father a baby while on this research study because the drugs in this study can affect a fetus.

If a woman becomes pregnant while on this research study or within 28 days after the last dose of study drug, she will be asked information concerning the outcome of her pregnancy. If a female partner of a male patient becomes pregnant while the male patient is on the study or within 28 days after the last dose of study drug, the pregnant female partner should be advised to call her healthcare provider immediately.

Women should not breastfeed a baby while on this research study.

It is important that you understand that you need to either practice “abstinence” (that is avoiding sexual activity) or use birth control while on this research study. Check with the study doctor about what types of birth control, or pregnancy prevention to use while in this study.

Contraception must be used for at least one week prior to the start of the research study and continuing for 5 months for women of child-bearing potential and 7 months for sexually active males after the last dose of the study drugs.

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

It is not possible to know at this time if the study drug(s)/study approach is better than the usual care for this cancer so this research study may or may not help you. But, this research 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. You will not lose medical care or any legal rights.

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

What are the costs of taking part in this study?

The nivolumab, ipilimumab, and GM-CSF will be supplied at no charge while you take part in this research study. It is possible that the nivolumab, ipilimumab, and GM-CSF 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 research study, including the cost of study drug preparation and administration, tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are being done at no charge. Before you decide to be in the research 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 research 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 research study and need medical treatment, please tell your study doctor. Contact information for your study doctor is listed on the consent cover page. The study sponsors will not offer to pay for medical treatment for

injury. Your insurance company may not be willing to pay for research study-related injury. If you have no insurance, you would be responsible for any costs.

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

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

Who will see my medical information?

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

The ECOG-ACRIN Cancer Research Group is conducting this study. ECOG-ACRIN is a cancer research group that conducts studies for the National Cancer Institute. Your doctor is a member of ECOG-ACRIN or another group that is participating in this study. To help protect your privacy, ECOG-ACRIN has obtained a Confidentiality Certificate from the Department of Health and Human Services (DHHS). With this Certificate, ECOG-ACRIN cannot be forced (for example, by court subpoena) to disclose information that may identify you in any federal, state or local civil, criminal, administrative, legislative or other proceeding. Disclosure will be necessary, however, upon request of DHHS for audit or program evaluation purposes.

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

- Montana Cancer Consortium
- ECOG-ACRIN Cancer Research Group and the drug companies supporting the study
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Food and Drug Administration and the National Cancer Institute in the U.S., and similar ones if other countries are involved in the study.

Optional Studies Section:

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

This part of the consent form is about optional studies that you can choose to take part in. You will not get health benefits from any of these studies. The researchers leading 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.

You may be asked to do an online survey regarding your tobacco use. Regardless if you have used tobacco or not, the information you provide is important to us. You will complete this survey online at 3 different timepoints (before the study treatment, 3 months from study entry, and 6 months from study entry), each taking you about 6 minutes to complete. To participate, you will be asked for your email address so we can send you a link to ECOG-ACRIN Systems for Easy Entry of Patient Reported Outcomes (EASEE-PRO).

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

I agree to participate in the tobacco survey.

YES **NO**

1. **Optional Sample Collections for Laboratory Studies and/or Biobanking for Possible Future Studies**

   Researchers are trying to learn more about cancer and other health problems. Much of this research is done using samples of 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.

   At this time, we are requesting that you allow the collection and submission of samples of tumor tissue and blood for research to learn more about your type of cancer and how the treatment affects you and the cancer.

   We are also requesting that you allow the storage of these samples for research projects that may be done at a later date. These samples will be stored in a "biobank". The Biobanks are run by ECOG-ACRIN staff and researchers and they are financially supported by the National Cancer Institute.

What is involved if you provide your samples for research?

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

1. About *seven* tablespoons of blood will be collected from a vein in your arm before you start treatment, week 12 of induction and week 24 of maintenance. Blood will be submitted for research and anything leftover will be sent to the Biobank. The blood will be collected at the same time as the blood to monitor your heath is collected. However, sometimes an additional stick may be done to collect the blood samples.

2. Tumor tissue from the central review (described above) and from on- and post- treatment biopsies (if performed) will be submitted for research and anything leftover will be sent to the Biobank. No additional procedures will be done to obtain the tissue.
3. Your samples and some related health information will be stored in the Biobank, along with samples and information from people who took part in this or other research studies. The samples will be kept until they are used up. Information from your medical record will be updated from time to time.
4. Only qualified researchers can submit a request to use the materials stored in the Biobanks. A committee of experts at ECOG-ACRIN, and/or the National Cancer Institute, will review each request to use the samples for research. All research projects using these samples will also be reviewed by an ethics or institutional review board to ensure that the request is necessary and proper. Researchers will not be given your name or any other information that could directly identify you.
5. Neither you nor your study doctor will be notified when research will be conducted or given reports or other information about any research that is done using your samples.
6. Results from the research may be placed in centralized storage systems call databases. It is possible that some of your genetic information and your health information may be placed in these databases. It is also possible that some of these databases may be public.

What are the possible risks in providing your samples for research?

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 is a risk that someone could trace the information in a central database back to you. Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.
4. In some cases, this information could be used to make it harder for you to get or keep a job or insurance. There are laws against the misuse of genetic information, but they may not give full protection. There can also be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a study. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

When my samples are used for research, 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 samples and health information. Any Biobank and ECOG-ACRIN staff with access to the list must sign an agreement to keep your identity confidential.
3. Researchers to whom ECOG-ACRIN sends your samples 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 of allowing my samples to be used for research?

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 associated with providing my samples for research?

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 about allowing my samples to be used for research?

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

What if I have more questions?

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

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

Samples for use in future research studies:

1. *May we have samples of your blood and, if available, tumor tissue from biopsies performed during and after your treatment?*

   I agree to provide additional samples for research.

   YES **NO**

2. May we keep any tissue leftover after the central review for future research?

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

YES **NO**

THIS IS THE END OF THE SECTION ABOUT OPTIONAL STUDIES.

Where can I get more information?

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

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

Who can answer my questions about this study?

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

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 Signature: _____

Date: _____

Signature of Person Obtaining Consent: _____

Date: _____

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