Study Title for Participants: Testing the addition of high-dose vitamin D3 to usual chemotherapy treatment and bevacizumab for untreated advanced colorectal cancer

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: A021703, Randomized double-blind phase III trial of vitamin D3 supplementation in patients with previously untreated metastatic colorectal cancer (SOLARIS) (NCT04094688)

Overview and Key Information

What am I being asked to do?

We are asking you to take part in a research study. 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 colorectal cancer.

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.

This study is conducted by the Alliance for Clinical Trials in Oncology, a national clinical research group supported by the National Cancer Institute. The Alliance is made up of cancer doctors, health professionals, and laboratory researchers, whose goal is to develop better treatments for cancer, to prevent cancer, to reduce side effects from cancer, and to improve the quality of life of cancer patients.

Why is this study being done?

This study is being done to answer the following question: Can we lower the chance of your colorectal cancer growing or spreading by adding a new 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 advanced 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 Food and Drug Administration (FDA) approved drugs. Sometimes, combinations of these treatments are used. One of the common combinations of drugs used to treat your type of cancer is a three-drug regimen that includes 5-fluorouracil (also called 5-FU), leucovorin, and oxaliplatin, also called "FOLFOX," plus the immune therapy drug, bevacizumab. Another common combination of drugs used to treat your type of cancer is a three-drug regimen that includes 5-fluorouracil (also called 5-FU), leucovorin, and irinotecan, also called "FOLFIRI," plus the immune therapy drug, bevacizumab. Your doctor can explain which treatment may be best for you. These treatments can reduce symptoms and may stop the tumor from growing for a few months or longer. The usual approach is proven to help patients with your health condition live longer.

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 either get high-dose vitamin D3 in combination with the usual chemotherapy and bevacizumab or you will get regular-dose vitamin D3 in combination with the usual chemotherapy and bevacizumab. You will continue treatment for 5 years starting from the time you enrolled on the study or until your disease gets worse, the side effects become too severe, or you decide to no longer participate.

After you finish your treatment, your doctor will continue to follow your condition and watch you for side effects. They will check you every 6 months for a maximum of five years starting from the time you enrolled on the study; if you stop treatment before the end of the 5-year period and before your cancer gets worse, these follow-up visits will occur in clinic every 2-4 months until your cancer gets worse or you reach the end of the 5-year treatment period.

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 high-dose vitamin D3 in combination with the usual chemotherapy and bevacizumab may not be as good as the usual approach (usual chemotherapy plus bevacizumab) for your cancer at shrinking or stabilizing your cancer.

There is also a risk that you could have side effects from the combination of drugs. These side effects may be worse and may be different than you would get with the usual approach (usual chemotherapy plus bevacizumab) for your cancer.

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

- Infection, especially when white blood cell count is low
- Bruising, bleeding
- Anemia which may cause tiredness, or may require blood transfusion
- Numbness, tingling or pain of the arms and legs
- Loss of appetite
- Diarrhea
- Nausea
- Vomiting

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

Benefits

There is evidence that high-dose vitamin D3 in combination with the usual chemotherapy and bevacizumab is effective in shrinking or stabilizing your type of cancer. It is not possible to know now if the addition of high-dose vitamin D3 to the usual approach (usual chemotherapy plus bevacizumab) will extend your time without disease compared to the usual approach (usual chemotherapy plus bevacizumab). 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. 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), drug company supporting the study (Pharmavite), or study sponsor (Alliance). 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 (usual chemotherapy plus bevacizumab) plus high-dose vitamin D3 to using the usual treatment plus regular-dose vitamin D3. The addition of high-dose vitamin D3 to the usual chemotherapy plus bevacizumab could shrink your cancer or 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 different approach is better, the same, or worse than the usual approach. To decide if it is better, the study doctors will be looking to see if the addition of high-dose vitamin D3 to usual approach can shrink or stabilize tumors for a longer period of time than regular-dose vitamin D3 and usual approach.

There will be about 400 people taking part in this study.

What are the study groups?

This study has two study groups. You and your doctor will not be told which group you are in.

- **Group 1**

  If you are in this group, you will get the usual drug regimen used to treat this type of cancer, either FOLFOX plus bevacizumab or FOLFIRI plus bevacizumab, plus a study drug called high-dose vitamin D3. You will get the usual drug regimen as an IV infusion through a vein in the arm on the first through third days of every cycle, and you will get the high-dose vitamin D3 as a capsule you take by mouth once a day on each day of every cycle. One cycle is defined as 14 days. You will be asked to keep a pill diary. Each time you visit the clinic, you must bring the pill diary, any remaining pills, and the pill bottle.

  For the first cycle of treatment only, you will take two vitamin D3 capsules by mouth once a day for each day of the cycle. Each of the capsules will contain the high-dose vitamin D3. The two capsules will look identical, and you will be given one pill bottle with 14 capsules in it and a second pill bottle with 100 capsules in it. Giving an initial higher dose of a drug at the beginning of treatment is called a "loading dose." This is

used to make sure you have enough of the drug in your body at a potentially effective level. After the first cycle of treatment, you will return both pill bottles, and you will be given back one vitamin D3 pill bottle to use starting with the second treatment cycle and all cycles thereafter.

You will not be able to get additional doses of the study drug. This study drug is not approved by the FDA for treatment of your disease.

There will be about 200 people in this group.

- **Group 2**

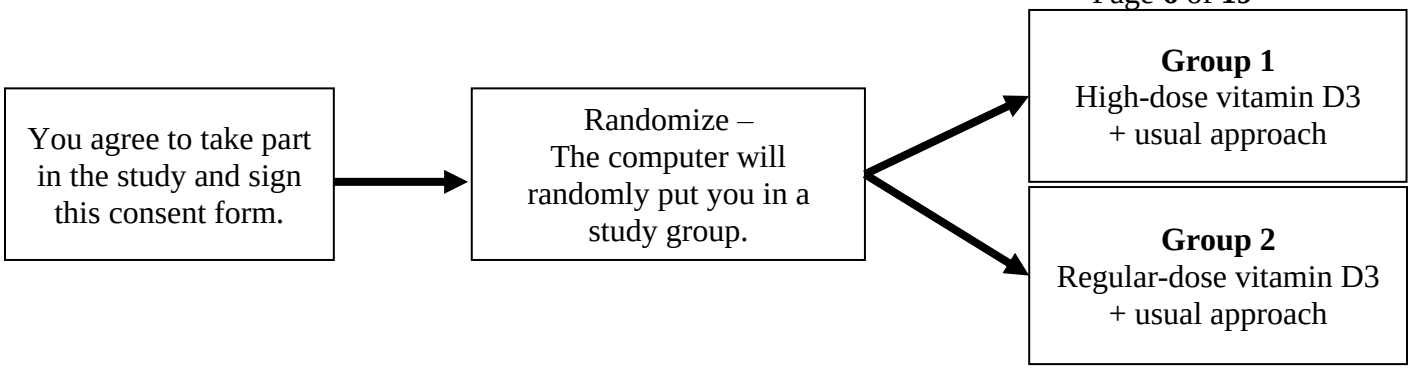
  If you are in this group, you will get the usual drug regimen used to treat this type of cancer, either FOLFOX plus bevacizumab or FOLFIRI plus bevacizumab, plus a study drug called regular-dose vitamin D3. You will get the usual drug regimen as an IV infusion through a vein in the arm on the first through third days of every cycle, and you will get the regular-dose vitamin D3 as a capsule you take by mouth once a day on each day of every cycle. One cycle is defined as 14 days. You will be asked to keep a pill diary. Each time you visit the clinic, you must bring the pill diary, any remaining pills, and the pill bottle.

  For the first cycle of treatment only, you will take two vitamin D3 capsules by mouth once a day for each day of the cycle. One of the capsules will contain the regular-dose vitamin D3, and one of the capsules will be a placebo. A placebo is a pill that looks like the study drug, but contains no medication. You will be given one pill bottle with 14 placebo capsules in it and a second pill bottle with 100 regular-dose vitamin D3 capsules in it. After the first cycle of treatment, you will return both pill bottles, and you will be given back one vitamin D3 pill bottle to use starting with the second treatment cycle and all cycles thereafter.

  You will not be able to get additional doses of the study drug. This study drug is not approved by the FDA for treatment of your disease.
  There will be about 200 people in this group.

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 chance of being in Group 1 or Group 2.

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 those exams, tests, and procedures that may not be needed with the usual approach, but are needed or are needed more frequently if you are in the study. The purpose of these procedures is to ensure your safety. We will use them to carefully monitor the effects of the study treatment, including preventing and managing side effects.

During study treatment, in addition to your doctor's usual safety review, you will be asked to complete the following assessments:

- A daily medication log where you will record the day, number of capsules taken, and the time of each dose of vitamin D3. You will be asked to bring the log (diary) with you to your clinic visits.

Some exams, tests, and procedures are a necessary part of the research study, but would not be included in usual care. Listed below are procedures that will be done for research purposes only.

You will need to have blood samples taken for this study. Additional needle sticks should not be needed for these blood samples. Approximately 1 teaspoon of blood will be collected before you start treatment, before you receive treatment on Day 1 of Cycle 5 and Cycle 9, and when you stop study treatment. These blood samples will be sent to the Alliance Biobank, and they will be used to determine the vitamin D3 levels in your blood. You and your doctor will not get the results of this testing.

If you are an English speaker and choose to take part in this study, you will be asked to fill out a form with questions about your diet and lifestyle. Researchers will use this information to learn more about how cancer and lifestyle affects people.

Since these forms are being used for research, the responses you provide will not be shared with your doctor. If you have any serious health issues or other concerns, please talk with your doctor or nurse right away.

You will be asked to fill out this form one time at the beginning of the study. The form will take 45-60 minutes to complete. The form will ask about things like your diet and daily habits. You don't have to answer any question that makes you feel uncomfortable. Your responses to the questions will be sent to the Diet and Lifestyle Questionnaire Team at Dana-Farber Cancer Institute after any information that could identify you (e.g. your name) has been removed.

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 usual approach plus high-dose vitamin D3 may not be as good as the usual approach at shrinking or 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 drug combination 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 6 months after you have completed the study.

Side Effect Risks

The drug combination 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 treatment.

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 (usual chemotherapy plus bevacizumab) plus a study drug (vitamin D3). 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 1 and Group 2 – Possible side effects of FOLFOX or FOLFIRI or bevacizumab are listed in the tables below. These drugs are part of the usual approach for treating this type of cancer:

Possible Side Effects of FOLFOX (Leucovorin, 5-Fluorouracil, Oxaliplatin)
(Table Version Date: November 14, 2016)

COMMON, SOME MAY BE SERIOUS In 100 people receiving FOLFOX (Leucovorin, 5-Fluorouracil, Oxaliplatin), more than 20 and up to 100 may have:
• Hair loss • Redness, pain or peeling of palms and soles • Rash, increased risk of sunburn, itching • Diarrhea, nausea, vomiting, constipation, loss of appetite • Difficulty swallowing • Sores in mouth • Heartburn • Infection, especially when white blood cell count is low • Anemia which may require a blood transfusion • Bruising, bleeding • Headache • Tiredness • Numbness, tingling or pain, "pins and needles" of the hands, feet, arms and legs • Tingling or a loss of feeling in your hands, feet, nose, or tightness in throat or jaw, or difficulty swallowing or breathing which may be made worse by exposure to cold • Cough • Fever, pain

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving FOLFOX (Leucovorin, 5-Fluorouracil, Oxaliplatin), from 4 to 20 may have:

- Chest pain
- Abnormal heartbeat which may cause fainting
- Swelling and redness at the site of the medication injection
- Hives
- Skin changes
- Weight gain, weight loss, belly pain
- Internal bleeding which may cause black tarry stool, blood in vomit or urine, or coughing up blood
- Changes in taste
- Blood clot which may cause swelling, pain, shortness of breath
- Bleeding from multiple sites including vaginal bleeding, bleeding of the testis, or bleeding of the brain
- Liver damage which may cause yellowing of eyes and skin
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Change in voice
- Confusion, dizziness
- Muscle weakness
- Inability to move shoulder or turn head
- Blurred vision, watering eyes
- Discomfort from light
- Abnormal body movement including the eye and eyelid
- Difficulty walking, using your hands, opening mouth, talking, with balance and hearing, smelling, eating, sleeping, emptying the bladder
- Hearing loss
- Swelling of the body which may cause shortness of breath
- Kidney damage which may require dialysis
- Scarring of the lungs
- Blockage of the airway which may cause shortness of breath, cough, wheezing
- Dehydration

RARE, AND SERIOUS

In 100 people receiving FOLFOX (Leucovorin, 5-Fluorouracil, Oxaliplatin), 3 or fewer may have:

- Damage to the heart which may cause shortness of breath
- A new cancer resulting from treatment of a prior cancer
- Redness, pain or peeling of palms and soles

Possible Side Effects of FOLFIRI (Leucovorin, 5-Fluorouracil, Irinotecan)
(Table Version Date: November 14, 2016)

COMMON, SOME MAY BE SERIOUS In 100 people receiving FOLFIRI (Leucovorin, 5-Fluorouracil, Irinotecan), more than 20 and up to 100 may have:
• Hair loss • Redness, pain or peeling of palms and soles • Rash, increased risk of sunburn, itching • Severe diarrhea, nausea, vomiting, constipation, loss of appetite, weight loss • Difficulty swallowing • Sores in mouth • Heartburn • Infection, especially when white blood cell count is low • Anemia which may require a blood transfusion • Bruising, bleeding • Headache • Tiredness, weakness, dizziness • Cough, shortness of breath • Fever, pain

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving FOLFIRI (Leucovorin, 5-Fluorouracil, Irinotecan), from 4 to 20 may have:
• Chest pain • Skin changes • Belly pain • Internal bleeding which may cause black tarry stools • Blood clot which may cause swelling, pain, shortness of breath • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Confusion • Difficulty with balancing • Abnormal eye movement, blurred vision, watering eyes • Discomfort from light • Scarring of the lungs

RARE, AND SERIOUS In 100 people receiving FOLFIRI (Leucovorin, 5-Fluorouracil, Irinotecan), 3 or fewer may have:
• Damage to the heart which may cause shortness of breath • A new cancer resulting from treatment of a prior cancer

Possible Side Effects of Bevacizumab
(Table Version Date: May 02, 2018)

COMMON, SOME MAY BE SERIOUS In 100 people receiving bevacizumab (rhuMAb VEGF), more than 20 and up to 100 may have:
• High blood pressure which may cause headaches, dizziness, blurred vision

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving bevacizumab (rhuMAb VEGF), from 4 to 20 may have:
• Anemia which may require blood transfusion • Low white cell count that may increase the risk of infection • Infection, including collection of pus in the belly or rectum • Abnormal heartbeat which may cause palpitations or fainting • Pain in the belly, rectum, chest, joints, muscles, or tumor • Low appetite, constipation, diarrhea, heartburn, nausea, vomiting, or dehydration • Bleeding from multiple sites including the vagina or nose • Internal bleeding which may cause black tarry stool, blood in vomit, coughing up blood, or blood in urine • Blockage of internal organs which may cause vomiting or inability to pass stool • Sores in the mouth • Allergic reaction during or after infusion of bevacizumab which may cause fever, chills, rash, itching, hives, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Delay in healing of wounds or spontaneous opening of wounds • Weight loss, tiredness, or dizziness • Muscle weakness • Damage to the jawbone which may cause loss of teeth • Headache • Numbness, tingling or pain in the fingers or toes • Hoarseness, stuffy nose, or cough • Dry skin • Swelling and redness of the skin • Blood clot in limbs or lungs which may cause swelling, pain, shortness of breath • Leakage of protein in the urine, which can rarely lead to damage to the kidney

RARE, AND SERIOUS In 100 people receiving bevacizumab (rhuMAb VEGF), 3 or fewer may have:
• Clots in the arteries, causing stroke (which may cause paralysis or weakness) or heart attack (which may cause chest pain or shortness of breath). This risk is significantly increased in patients who are elderly or with history of diabetes. • Heart failure which may cause shortness of breath, swelling of ankles, and tiredness

RARE, AND SERIOUS In 100 people receiving bevacizumab (rhuMAb VEGF), 3 or fewer may have:
• Bowel perforation (a tear in the bowel) that can cause pain or bleeding and require surgery to repair • A tear or hole (fistula) in internal organs such as the nose, throat, lungs, esophagus, rectum, or vagina. These conditions may cause serious infections or bleeding and require surgery to repair. • Sores in the throat • Flesh-eating bacteria syndrome, an infection in the deep layers of skin • Damage to organs (bone, lungs, others) which may cause loss of motion • Bleeding in the tumor, brain, belly or lungs which may cause confusion, blood in stool or coughing up blood • Brain damage which may cause headache, seizure, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome) • Kidney damage which may require dialysis • Redness, pain or peeling of palms and soles

Study Group 1 and Group 2 – Possible side effects of vitamin D3 are listed in the table below.

Possible Side Effects of Vitamin D3
(Version Date: November 20, 2018)

COMMON, SOME MAY BE SERIOUS
• Muscle weakness • Tiredness • Nausea, vomiting, constipation • Loss of appetite

RARE, AND SERIOUS
• Pain in bone • Loss of bone tissue • Increased urination • Kidney damage, which may cause swelling, may require dialysis • Kidney stones • Weight loss

Additional Drug Risks

Additional notes on possible side effects for bevacizumab:

- Risk in children or adolescents: abnormal bone changes which may interfere with growth
- Risk in pre-menopausal women: more likely to develop menopause when taking bevacizumab

The study drug could interact with other drugs or supplements, as well as with certain foods and beverages. You should not take other drugs that contain calcium or vitamin D, and you should drink/eat milk, orange juice, yogurt, or cereal in moderation while on study treatment.

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 6 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 study treatment 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 and/or your insurance provider will not have to pay for exams, tests, and procedures done for research purposes only or that are covered by the study. These include:

- The extra blood samples before you start treatment, before you receive treatment on Day 1 of Cycle 5 and Cycle 9, and when you stop study treatment.

You or your insurance provider will not have to pay for the vitamin D3 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. Contact information for your study doctor is listed on the consent cover page. 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.

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. 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 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:

- Montana Cancer Consortium
- The study sponsor and any company supporting the study or the study agent now or in the future, and any of its agents.
- The Diet and Lifestyle Questionnaire Team at Dana-Farber Cancer Institute
- The 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 including the Imaging and Radiation Oncology Core (IROC).
- The Alliance for Clinical Trials in Oncology Foundation and the groups it works with, including Alliance Foundation Trials, LLC and its research partners, is collaborating with the sponsor and a select number of NCTN institutions on a special project called ICAREdata™. Please ask your study team if this will pertain to you. The ICAREdata™ project will be collecting data from the electronic medical record. This information will be stored in a secured location. Please ask your study doctor if you have any questions.

Your study records also will be stored for future use. However, your name and other personal information will not be used. Some types of future research may include looking at your records and those of other patients to see who had side effects across many studies or comparing new study data with older study data. However, 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 information for your study doctor is listed on the consent cover page.

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.

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 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, blood samples while you are on study, a sample of tissue from your previous biopsy or surgery, and stool samples while you are on study will be collected and stored. Storing samples for future studies is called "biobanking." The biobank is being run by the Alliance for Clinical Trials in Oncology and is supported by the NCI. 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.

We don't know what research may be done in the future using your blood, tissue, and/or stool 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.
- Future research studies may include sequencing of all or part of your DNA called genomic sequencing. All your genetic information makes up your genome. Genomic sequencing is a test that records all or part of the pieces of DNA that are in your genes, piece by piece. This is usually done to look for changes in your genome that may cause health problems.
- You will not get reports or other information about any research that is done using your samples.

What is involved in this optional sample collection?

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

1. About 3 tablespoons of blood will be collected from a vein in your arm before you start treatment, before you receive treatment on Day 1 of Cycle 5 and Cycle 9, and when you stop treatment. A sample from the tissue that was collected at the time of your previous surgery or biopsy will be sent to the biobank. A stool sample will be collected before you start treatment, before you receive treatment on Day 1 of Cycle 3 and Cycle 5, and when you stop treatment.
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. No additional needle sticks should be needed as these blood samples will be collected at the same time as the blood samples required for the main study.
- 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, who will let the biobank know. Contact information for your study doctor is listed on the consent cover page. 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. Contact information for your study doctor is listed on the consent cover page.

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 to have my blood and tissue collected, and I agree that my blood and tissue samples and related health information may be kept in a biobank for use in future health research.

YES NO

I agree to have my stool collected, and I agree that my stool 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 Signature: _____

Date: _____

Signature of Person Obtaining Consent: _____

Date: _____

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