A Phase 2 Study of Savolitinib in Subjects with MET Amplified Metastatic Colorectal Cancer

Trial: NCT03592641

Pre-Screening Consent Form

December 3, 2020

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Main Consent Form

December 3, 2020

Screening Consent FormStudy Title for Study Participants: Testing the effects of savolitinib in metastatic colorectal cancer with MET gene changes.

Official Study Title for Internet Search on http://www.ClinicalTrials.gov:
Protocol 10181**,** A Phase 2 Study of Savolitinib in Subjects with MET Amplified Metastatic Colorectal Cancer (NCT# 03592641)

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 study because you have metastatic colorectal cancer that has spread to other parts of your body, and your cancer has a change in the gene called MET.

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 screening study being done?

The purpose of the screening study is to test your blood to see if you may be eligible for the main study testing savolitinib. That study is being done to learn if savolitinib can shrink tumors in patients with metastatic colorectal cancer with the MET gene change (amplification). In order to participate in the main study, we will need to show that your blood has a MET gene amplification. The Guardant 360^{TM} test used to determine eligibility for the main study is not FDA approved for this purpose.

There will be about 150 people taking part in the screening study.

What is the usual approach to my metastatic colorectal cancer?

You are being asked to take part in this screening study because you have metastatic colon cancer. People who are not in a study are usually treated with either surgery, radiation, or with drugs, such as regorafenib or TAS-102 if you have not received either of them. Both regorafenib

and TAS-102 are FDA approved treatment for metastatic colorectal cancer. Sometimes, combinations of surgery, radiation and/or drugs are used and your study doctor can explain which may be best for you. These treatments can reduce symptoms and may stop the tumor from growing for several months or more.

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 screening study, you will have a blood draw.

You will be part of the screening study for only the time required to perform the Guardant 360™ blood test for *MET* gene amplification. Your blood will be collected in the clinic and sent to a lab company to be tested called Guardant Health. The blood tubes and paperwork sent to Guardant Health for your blood test will not include any of your personal information. The results will be available in about two weeks and the Lead Study Principal Investigator will send the results to your study doctor who will discuss them with you at that time.

If your blood has the *MET* gene amplification, he or she will discuss the clinical study in more detail and present you the main study informed consent as a separate document.

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 screening study, there is a risk that:

- Taking a blood sample may cause some discomfort. There may be slight pain, a small amount of bleeding, discoloration or bruising at the site where the needle is inserted. You may become dizzy or faint. Very rarely, irritation of a vein caused by a small blood clot or infection of the vein can develop. Care will be taken to avoid this.
- You may be asked sensitive or private questions which you normally do not discuss

Guardant 360™ assay is being used to determine eligibility for this trial and is not approved by the U.S. Food and Drug Administration for this indication.

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

Benefits

This screening study will help determine whether you could be eligible for the main study.

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

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 testing on your sample can be stopped.

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 screening 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.
- The study is stopped by the Institutional Review Board (IRB), or U.S. Food and Drug Administration (FDA), or study sponsor (National Cancer Institute or NCI). The study sponsor is the organization who oversees the study.

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

What is the purpose of this study?

The purpose of this screening study is to test for the presence of *MET* gene amplification.

There will be about 150 people taking part in this screening study.

What are the study groups?

The screening study does not have any study groups.

More details will be provided to you in the main study consent if your blood has the specific gene change called *MET* gene amplification.

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

You will be asked to provide a blood sample (about 4 teaspoons) for this screening study.
To have your blood tested for the *MET* gene amplification, your gender, cancer diagnosis, and blood collection date and time will be included on a form and shipped with your blood sample to Guardant Health. Guardant Health will not receive any of your personal information. Guardant Health is the lab company that will be testing the blood sample collected from you. In addition

to checking for the *MET* gene amplification, the blood test provides other information about gene changes that may be useful to you and your study doctor.

The Lead Study Principal Investigator will send your study doctor a copy of the Guardant 360™ blood test results to include in your medical record.

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

General Risks

You 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.

Gene Testing Risks

As part of this study, we are also studying a gene test. Because this gene test is still being studied, there is a risk that the test results may be wrong. If the test results are wrong, you may be included in this study even though it may not offer the best treatment option for you. Or, you may not be included in this study even though it may offer a good treatment option for you.

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.

What are the costs of taking part in this screening study?

You and/or your health plan/insurance company will not need to pay for the cost of doing the Guardant 360™ blood test.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale.

What happens if I am injured because I took part in this screening 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. The study sponsors will not pay for medical treatment for injury. Your insurance company may not be willing to pay for study-related injury. Ask them if they will pay. If you have no 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 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 the results of the Guardant360 test from this screening study will be kept in a central database for research. Your name or contact information will not be put in the database. The Lead Study Principal Investigator will have access to the database. A copy of the Guardant360 blood test results will be shared by the Lead Study Prinicipal Investigator with your study doctor. If the 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:

- The study sponsor and any company supporting the screening study now or in the future.
- 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.

There are laws that protect your genetic information. However, there is a risk that someone could get access to your genetic information and identify you by name. In some cases, employers could use your genetic information to decide whether to hire or fire you. The study doctors believe the risk of this happening is very small. However, the risk may increase in the future as people find new ways of tracing information. For more information about the laws that protect you, ask your study doctor.

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.

My Signature Agreeing to Take Part in the Screening 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 screening study

Participant's signature_____

Date of signature_____

Signature of person(s) conducting the informed consent discussion_____

Date of signature_____

Research Study Informed Consent Document

Study Title for Study Participants: Testing the effects of savolitinib in metastatic colorectal cancer with MET gene changes.

Official Study Title for Internet Search on http://www.ClinicalTrials.gov:
Protocol 10181, A Phase 2 Study of Savolitinib in Subjects with MET Amplified Metastatic Colorectal Cancer (NCT# 03592641)

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 study because you have metastatic colorectal cancer that has spread to other parts of your body, and your cancer has a change in the gene called MET.

Taking part in this study is your choice.

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

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

Why is this study being done?

This study is being done to answer the following question:

Can we lower the chance of your colorectal cancer growing or spreading by using a new drug?

We are doing this study because we want to find out if this approach is better or worse than the usual approach for your metastatic colorectal cancer. The usual approach is defined as care most people get for metastatic colorectal cancer who have tried all treatments that are approved by the U.S. Food Drug Administration (FDA).

What is the usual approach to my metastatic colorectal cancer?

You are being asked to take part in this study because you have metastatic colon cancer. People who are not in a study are usually treated with either surgery, radiation, or with drugs, such as regorafenib or TAS-102 if you have not received either of them. Both regorafenib and TAS-102 are FDA approved treatment for metastatic colorectal cancer. Sometimes, combinations of surgery, radiation and/or drugs are used and your study doctor can explain which may be best for you. These treatments can reduce symptoms and may stop the tumor from growing for several months or more.

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 get the study drug, savolitinib, until your disease gest worse or the side effects become too severe.

If you finish the study drug for any reason other than disease progression, your doctor will ask you to return to the clinic for routine evaluations until your cancer gets worse or you start a new anti-cancer therapy. These follow up visits will continue until 2 years after the last patient of this study starts the study drug.

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 the study drug 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. These side effects may be worse and may be different than you would get with the usual approach for your cancer.

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

- Nausea, vomiting
- Tiredness
- Anemia which may require blood transfusion
- Constipation, diarrhea
- Swelling of arms, legs
- Fever
- Liver damage which may cause yellowing of the eyes and skin
- Loss of appetite

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

Benefits

This study drug has shrunk (decreased the size of the tumor) or stabilized (no change in the size of the tumor) in a limited number of people with other types of cancer that carry a specific gene change called *MET* gene amplification. It is unlikely that it will work in everyone with your type of cancer or help you live longer. This study may help the study doctors learn things that may help other 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 Institutional Review Board (IRB), or U.S. Food and Drug Administration (FDA), or study sponsor (National Cancer Institute or NCI). The study sponsor is the organization who oversees the study.

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

What is the purpose of this study?

The purpose of this study is to test any good and bad effects of the study drug called savolitinib. Savolitinib could shrink your cancer, but it could also cause side effects, which are described in the risks section below. The study doctors hope to learn if the study drug will shrink the cancer by at least one quarter compared to its present size. Savolitinib has not been approved by the U.S. Food and Drug Administration (FDA) in the treatment of any cancer. It has not been tested in colorectal cancer, but has shrunk tumors in patients with stomach, lung, and ovarian cancers.

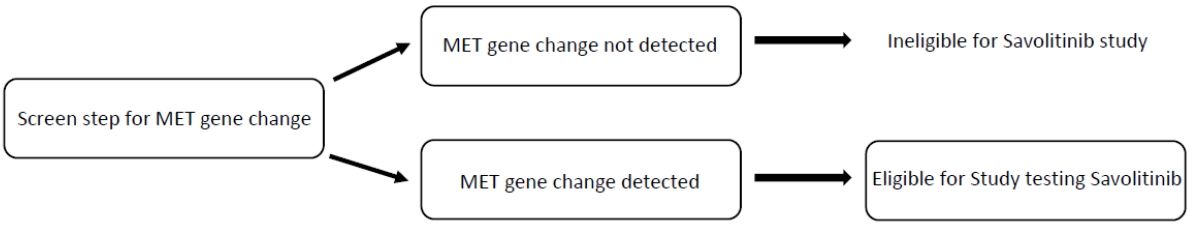
There will be about 15 people taking part in this study.

Another purpose of this study is for researchers to learn if the results of the MET gene test (used to determine your eligibility for this study) can help to predict which future patients may benefit from the study drug.

What are the study groups?

This study has a screening step. The purpose of this step is to test your blood to find out if it has a gene change called MET gene amplification. If it does and you meet all the study requirements, then you can choose to take part in the study testing savolitinib. If we find that your blood does not show the MET gene change, then your doctor will discuss other options for your care. This blood screening test is not approved by the FDA in your disease

The following picture also shows what will happen if you take part in the study. Read the illustration from left to right. The following illustration also shows when the study drugs are given. Read the illustration from left to right.



In this study, you will get the study drug, savolitinib, as tablets you take by mouth once per day of each cycle. Each cycle is 28 days. You will repeat each cycle until your cancer gets worse or have difficulty tolerating the study drug. See study calendar for more information.

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.

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.

Before you begin the study

Prior to starting the study drug, you will have a blood sample (about 4 teaspoons) taken to look at additional gene changes and protein markers that might predict response to treatment.

Finding these changes would not affect your treatment in this study. However, they could affect your health in other ways. It is possible that tests on blood samples will identify information about you that was previously unknown, such as disease status or risk. There are no plans to provide this information to you or your treating physician unless the information indicates that you may be at risk for a disease known at the time of testing to potentially cause premature death if untreated. In that case, the lead investigator for this study will notify your treating physician, so that your treating physician can speak with you directly. No information will be provided in a voice mail, email, or otherwise prior to contacting you. Please notify us of any change in your contact information.

During the study

You will have research-related blood samples taken on Day 1 prior to starting study drug and Day 15 of the first 28-day cycle of the study drug. Samples will also be taken on day 1 of every other cycle beginning with cycle 3, (cycles, 3, 5, 7, and so on), and when you finish the study drug. These sample are needed to look at factors in the blood that might show a response to the study drug.

A patient study calendar is attached at the end of this document. It shows how often these research samples will be done.

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 savolitinib (AZD6094) may not be as good as the usual approach for your cancer or condition 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 savolitinib (AZD6094) 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.

Gene Testing Risks

As part of this study, we are also studying a gene test. Because this gene test is still being studied, there is a risk that the test results may be wrong. If the test results are wrong, you may be included in this study even though it may not offer the best treatment option for you. Or, you may not be included in this study even though it may offer a good treatment option for you.

Blood Drawing Risks

Taking a blood sample may cause some discomfort. There may be slight pain, a small amount of bleeding, discoloration or bruising at the site where the needle is inserted. You may become dizzy or faint. Very rarely, irritation of a vein caused by a small blood clot or infection of the vein can develop. Care will be taken to avoid this.

Side Effect Risks

The savolitinib (AZD6094) 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 side effects from the study drug(s)/study approach.

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.

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.

Possible Side Effects of Savolitinib (AZD6094)
(Table Version Date: April 2, 2020)

COMMON, SOME MAY BE SERIOUS In 100 people receiving savolitinib (AZD6094), more than 20 and up to 100 may have:
• Nausea, vomiting • Swelling of arms, legs • Tiredness

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving savolitinib (AZD6094), from 4 to 20 may have:
• Anemia which may require blood transfusion • Constipation, diarrhea • Swelling of arms, legs • Fever • Liver damage which may cause yellowing of the eyes and skin • Loss of appetite • Cough

RARE, AND SERIOUS In 100 people receiving savolitinib (AZD6094), 3 or fewer may have:
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Change in heart rhythm • Severe skin rash with blisters and peeling which can involve mouth and other parts of the body

Note: Deaths have occurred to participants in prior savolitinib studies. In 100 people receiving savolitinib, 1 or fewer may have died from effects possibly related to this study drug.

Additional Drug Risks

The study drug could interact with other drugs and certain foods. Your study doctor will give you a drug information handout and wallet card that lists these possible interactions. Share this information with your family members, caregivers, other health care providers, and pharmacists.

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

During savolitinib therapy and for 4 weeks after the last dose you should avoid prolonged exposure to the sun, wear protective clothing and a hat, and seek shade from the sun as far as possible; you should also use a sunscreen with SPF 30+. Exposure to sunbeds and tanning booths should also be avoided.

REMINDER: Report with no delay the symptoms listed in the table above. Some of the symptoms can indicate a very serious side effect that could require a change to the dose or the schedule of the savolitinib

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 study drug 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. You should refrain from donating sperm from the start of dosing until 6 months after discontinuing study drug. **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 metastatic colorectal 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.
- 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:

- Research blood collections prior to starting study drug, at Cycle 1 Day 15, on day 1 of every other cycle beginning with cycle 3, (cycles, 3, 5, 7, and so on), and when you finish the study drug

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

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 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.
- 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.
- Monitors and auditors.
- Institutions/companies and associated laboratories affiliated with the study sponsor.

There are laws that protect your genetic information. However, there is a risk that someone could get access to your genetic information and identify you by name. In some cases, employers could use your genetic information to decide whether to hire or fire you. The study doctors believe the risk of this happening is very small. However, the risk may increase in the future as people find new ways of tracing information. For more information about the laws that protect you, ask your study doctor.

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).*

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

Optional studies that you can choose to take part in

This part of the consent form is about optional studies that you can choose to take part in. They are separate from the main study described above. These optional studies will not benefit your health. The researchers leading these optional studies hope the results will help other people

with cancer in the future. The results will not be added to your medical records and you or your study doctor will not know the results.

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

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

Optional sample collections for known laboratory studies and/or storage for possible future studies

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

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

Known future studies

If you choose to take part in this optional study, researchers will collect tissue for research as indicated below:

If available, a small piece of tumor tissue from your previous surgery and/or biopsy (archival tissue sample) will be obtained for research tests to look for some specific gene changes or markers in the cancer cell that might predict response to treatment.

Unknown future studies

If you choose to take part in this optional study, any leftover tissue after known studies are completed will be collected and stored. Storing samples for future studies is called "biobanking." The biobank is being run by ETCTN Biorepository 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 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.

- 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. 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.
2. 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.
3. 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?

- Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find new ways of tracing information.
- In some cases, this information could be used to make it harder for you to get or keep a job and get or keep health insurance. There are laws against the misuse of genetic information, but they may not give full protection. For more information about the laws that protect you, ask your study doctor or visit: https://www.genome.gov/10002328/

How will information about me be kept private?

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

1. They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information.
2. Researchers who study your sample and information will not know who you are. They also must agree that they will not try to find out who you are.
3. Your personal information will not be given to anyone unless it is required by law.

4. If research results are published, your name and other personal information will not be used.

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

You will not benefit from taking part.

The researchers, using the samples from you and others, might make discoveries that could help people in the future.

Are there any costs or payments to this optional sample collection?

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

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

If you decide you no longer want your samples to be used, you can call the study doctor, *(insert name of study doctor for main trial)*, at *(insert telephone number of study doctor for main trial)*, who will let the biobank know. Then, any sample that remains in the biobank will be destroyed or returned to your study doctor. This will not apply to any samples or related health information that have already been given to or used by researchers.

What if I have questions about this optional sample collection?

If you have questions about the use of your samples for research, contact the study doctor, *(insert name of study doctor for main trial)*, at *(insert telephone number of study doctor for main trial)*.

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

Samples for known future studies:

I agree that my samples and related health information may be used for the laboratory study described above.

YES NO

Samples for unknown future studies:

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

YES NO

Contact for Future Research

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to participate in other research in the future.

YES NO

This is the end of the section about optional studies.

My signature agreeing to take part in the study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed and dated copy of this form. I agree to take part in the main study. I also agree to take part in any optional studies where I circled "yes".

Participant's signature _____

Date of signature _____

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

Date of signature _____

Patient Study Calendar

	Patient Activity
Before the Study	
Pre-Study/Screening	You will need to have the following tests and procedures to find out if you can be in the study: **Routine:** • Medical history • Physical exam - vital signs, weight, height, performance status • Review of current medications and supplements • Echocardiogram (EKG) to test your heart • Tumor measurements by x-ray, CT, MRI, or PET • Blood test - blood count, chemistry, and liver function - tumor marker called CEA • Urine test • Pregnancy test (if you are a woman who is able to become pregnant) **Research-related:** • OPTIONAL: Archived tumor collection from a previous surgery or biopsy
During the Study	
Cycle 1 Day 1	**Routine (prior to starting study drug):** • Physical exam - vital signs, weight, performance status • Review of current medications and supplements • Blood test - blood count, chemistry, and liver function • Urine test **Research-related (prior to starting study drug):**

	Patient Activity
	• Blood collection for pharmacogenomics, cell-free tumor DNA and circulating proteins (about 4 teaspoons) ****Start taking savolitinib by mouth once daily****
Cycle 1 Day 15	**Routine:** • Physical exam - vital signs, weight, performance status • Review of current medications and supplements • Blood test - blood count, chemistry, and liver function • Urine test • Review of side effects **Research-related:** • Blood collection for cell-free tumor DNA and circulating proteins (about 3 teaspoons)
Cycle 2 and all cycles following (ie., Cycle 3, 4, 5, 6, etc)	**Routine:** • Physical exam - vital signs, weight, performance status • Review of current medications and supplements • Blood test - blood count, chemistry, and liver function - tumor marker called CEA • Urine test • Review of side effects
On day 1 of every other cycle beginning with cycle 3, (cycles, 3, 5, 7, and so on)	**Routine:** • Echocardiogram (EKG) to test your heart • Tumor measurements by x-ray, CT, MRI, or PET **Research-related:** • Blood collection for cell-free tumor DNA and circulating proteins (about 3 teaspoons)
End of Study Drug	**Routine:** • Physical exam - vital signs, weight, performance status

	Patient Activity
	• Echocardiogram (EKG) to test your heart • Blood test - blood count, chemistry, and liver function • Urine test • Review of side effects **Research-related (prior to starting study drug):** • Blood collection for cell-free tumor DNA and circulating proteins (about 3 teaspoons)
Off Study	
Follow-Up	**Routine:** • Physical exam - vital signs, weight, performance status • Echocardiogram (EKG) to test your heart • Blood test - blood count, chemistry, and liver function • Urine test • Review of side effects