SUMMARY OF CHANGES – Consent

NCI Protocol #: 10387
Local Protocol #: 21-059
Protocol Version Date: 04/10/24

Protocol Title: Pilot Trial of Nivolumab Plus Cabozantinib for Advanced Solid Tumors in Patients with HIV Infection

Informed Consent Version Date: April 10, 2024

I. Comments Requiring a Response– Administrative & Editorial Issues:

#	Section	Change
1.	Patient Study Calendar	Integrated the patient study calendar with the existing protocol

Research Study Informed Consent Document

Study Title for Participants: Testing the combination of the anti-cancer drugs XL184 (cabozantinib) and nivolumab in patients with advanced cancer and HIV

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: "Protocol 10387, Pilot Trial of Nivolumab plus Cabozantinib for Advanced Solid Tumors in Patients with HIV infection" (NCT04514484)

Overview and Key Information

What am I being asked to do?

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

We are asking you to take part in this research study because you have advanced cancer and are undergoing treatment for HIV.

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:

Is it safe and tolerable to give nivolumab in combination with XL184 (cabozantinib) in patients with advanced cancer and HIV?

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

This is the first time these two drugs will be tested together in patients with advanced cancer that also have HIV.

What is the usual approach to my advanced solid tumor?

The usual approach for patients who are not in a study is treatment with surgery, radiation, or drugs including chemotherapy or immunotherapy that are FDA-approved. Sometimes, combinations of these treatments are used. 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 combination of nivolumab and XL184 (cabozantinib) is not FDA approved for any cancer.

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 XL184 (cabozantinib) for 2 weeks, followed by a combination of XL184 (cabozantinib) and nivolumab for up to 1 year, or 6 months to 1 year until your tumor gets worse, your study doctor believes it is no longer working for you, you cannot tolerate the drugs, or you desire to discontinue the study drugs.

You may be asked to change the medication that you are taking for your HIV to avoid possibly harmful medication interactions between the study agent and your HIV medication. You should receive appropriate care and treatment for your HIV infection under the care of a physician experienced in HIV management. You will be eligible if there is no intention to initiate therapy or your HIV treatment has been stable for at least 4 weeks with no intention to change the regimen within 8 weeks following study entry.

Under appropriate care, the change of your HIV medication should minimally impact the control of your HIV infection.

After you finish XL184 (cabozantinib) and nivolumab your doctor will continue to follow your condition for 16 more weeks and watch you for side effects, your cancer's response to the medications, and any effects of the medications on HIV. This means you will keep seeing your doctor each month for approximately 4 months after you finish taking the study drugs.

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 combination of nivolumab and XL184 (cabozantinib) 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 nivolumab and XL184 (cabozantinib). These side effects may be worse and may be different than you would get with the usual approach for your cancer. Combining the study drugs can result in greater similar side effects of those currently experienced by each drug individually.

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

- Diarrhea, nausea, vomiting
- Rash
- Tiredness
- Weight loss, loss of appetite
- Changes in taste
- Redness, pain or peeling of palms and soles
- High blood pressure which may cause headaches, dizziness, blurred vision

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

Benefits

There is some evidence in people not undergoing treatment for HIV that treatment with XL184 (cabozantinib) in combination with nivolumab can shrink or stabilize cancer but we do not know if this will happen in people being treated for HIV. It is unlikely that being treated with the combination of XL184 (cabozantinib) and nivolumab will 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), Food and Drug Administration (FDA), or study sponsor (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 the safety and tolerability (side effects) of a combination of drugs called XL184 (cabozantinib) and nivolumab in people with cancer that are undergoing treatment for HIV. This drug combination has been tested in people with cancer not undergoing treatment for HIV. There will be about 18 people taking part in this study.

XL184 (cabozantinib) and nivolumab have both already been approved by the FDA to treat other cancers.

These chemotherapy drugs, XL184 (cabozantinib) and nivolumab have already approved by the FDA individually for use in cancers including bladder, head and neck, thyroid, liver, kidney, lung, and colon cancer, in addition to certain types of skin cancer and lymphoma. The combination of XL184 (cabozantinib) and nivolumab has not been approved by the FDA and are considered investigational when used in combination and when used in patients who are also undergoing treatment for HIV. In some of these cases, it is not used until other therapies stop working.

Another purpose of this study is to see how the combination of XL184 (cabozantinib) and nivolumab affect the medication you are on for your HIV.

What are the study groups?

There are two parts in this study, a safety run-in part and a dose expansion part. Your doctor will tell you which part you are in.

In the safety run-in part of this study, people will receive doses of the study drugs, XL184 (cabozantinib) and nivolumab, that are recommended for patients not being treated for HIV.

The first 3 people taking part in this study will get the recommended dose for patients not being treated for HIV. If the drugs do not cause serious side effects, 3 more people will be treated with this dose level. If the drugs do not cause serious side effects in this group, the dose expansion part of this study begins. If the study therapy does cause serious side effects, the study will be stopped.

In the dose expansion part of this study, the highest dose with manageable side effects will be given to 12 more people with Kaposi sarcoma. This will help study doctors better understand the side effects that may happen with this drug.

Treatment schedule: You will first get XL184 (cabozantinib) as a tablet you take by mouth once a day for 14 days. Then you will receive XL184 (cabozantinib) as a tablet you take by mouth once a day and nivolumab through a vein in your arm on Day 1 of each cycle. Each cycle is 28 days. Do not take XL184 (cabozantinib) with food. Do not eat for at least 2 hours before and at least 1 hour after taking XL184 (cabozantinib). Swallow tablets whole with a full glass of water. Do not crush XL184 (cabozantinib) tablets. If a dose is missed, and your next dose is less than 12 hours, take your next dose at the normal time. Do not make up the missed dose. See the study calendar for more information.

You will not be able to get additional doses of these drugs. These drugs are not approved by the FDA for treatment of your disease.

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

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

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

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

- Blood counts done every other week during the first two cycles of treatment and the first week of every cycle after that..
- Thyroid testing done the first week of cycle
- Physical exams done every other week during the first cycle.

- Blood collection to see your CD4, CD8 blood counts and your HIV viral load before you begin study treatment, on Day 1 of cycle 1, on Day 1 of Cycle 3, Day 1 of Cycle 5, and then every 12 weeks, and when you stop study treatment.

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 have photographs of your lesions before you begin study treatment, if you have a response to the study treatment, and at your finial visit after you finish study treatment.

A patient study calendar is attached at the end of this document. It shows how often these procedures 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 study drugs may not be as good as the usual approach for your cancer 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 study drugs used in this study could be very harmful to an unborn or newborn baby. There may be some risks that doctors do not yet know about. It is very important that you check with your study doctor about what types of birth control or pregnancy prevention to use during the study and for 5 months (for women) or 7 months (for men) after you have completed the study.

This study will use a sample of your tissue. Generally, your hospital will keep some of your tissue. This tissue may be used to help treat your cancer in the future. Because this study will need to use some of this tissue, there is a small risk that it could be used up.

Blood Draw Risks

Some of the risks from drawing blood from your arm may include pain, bruising, light-headedness, and rarely, infection. For most people, needle punctures to get blood samples do not cause any serious harm. 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.

Side Effect Risks

The study drugs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and let you know if changes occur that may affect your health.

There is also a risk that you could have other side effects from the study drugs.

Here are important things to know about side effects:

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 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 in patients with HIV. This may increase your side effects or may cause new side effects.
You should notify your doctor immediately at the first sign of poorly formed or loose stools or an increased frequency of bowel movements. Loperamide (Imodium) should be kept on hand and should be taken as recommended by your doctor.

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 Nivolumab
(CAEPR Version 2.5, June 10, 2023)

Special precautions Side effects of Nivolumab may happen anytime during treatment or even after your treatment has ended. Some of these problems may happen more often when Nivolumab is used in combination with ipilimumab. **Call or see your healthcare provider right away if you develop any problems listed below or the symptoms get worse.**
COMMON, SOME MAY BE SERIOUS In 100 people receiving nivolumab, more than 20 and up to 100 may have:
• Tiredness

OCCASIONAL, SOME MAY BE SERIOUS
In 100 people receiving nivolumab, from 4 to 20 may have:

- Anemia which may require blood transfusion
- Swelling and redness of the eye
- Swelling of arms and legs which may cause a feeling of heaviness and tightness
- Pain
- Diarrhea, nausea
- Dry mouth
- Fever
- Swelling and redness at the site of the medication injection
- Bruising, bleeding
- Pain or swelling of the joints
- Loss of appetite
- Reaction during or following a drug infusion which may cause fever, chills, rash

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

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

RARE, AND SERIOUS In 100 people receiving nivolumab, 3 or fewer may have:
• Swelling of arms and legs which may cause a feeling of heaviness and tightness • Dry eyes • Sores in the mouth which may cause difficulty swallowing • A syndrome starting with flu-like symptoms and followed by swelling, tenderness which may cause flu-like symptoms, blurred vision, ringing in the ears, changes in hair or hair loss • Swelling of the bowels Nivolumab may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to: • Visual disturbances which may cause double vision, blurred vision, or loss of vision with a chance of blindness • A condition with high blood sugar which leads to tiredness, frequent urination, excessive thirst, headache, nausea and vomiting, and can result in coma • Kidney problems, including nephritis and kidney failure requiring dialysis. Signs of kidney problems may include: decrease in the amount of urine, blood in your urine, ankle swelling. • Heart problems including swelling and heart failure. Symptoms and signs of heart problem may include: Shortness of breath, swelling of the ankle and body. • Problem of the muscle, including swelling, which can cause muscle pain and severe muscle weakness sometimes with dark urine • Swelling of the brain (meningitis/encephalitis) which may cause: headache, stiff neck confusion, sleepiness, seizures or injury to the brain which may cause headache, seizure, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome) • Problem of the nerves that can cause paralysis. Signs and symptoms may include: numbness, tingling of hands and feet; weakness of the arms, legs and facial muscle movement • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Complications associated with stem cell transplant using donor stem cells (allogeneic stem cell transplant). These complications are caused by attack of donor cells on the host organs (inducing liver, skin and gut damage), and can lead to death. If you are considering an allogeneic stem transplant after participating in this study, please tell your doctor that you have received Nivolumab therapy, since the risk and severity of transplant-associated complications may be increased.

Possible Side Effects of XL184 (cabozantinib)
(Table Version Date: December 17, 2018)

COMMON, SOME MAY BE SERIOUS In 100 people receiving XL184 (cabozantinib), more than 20 and up to 100 may have:

- Diarrhea, nausea, vomiting
- Tiredness
- Weight loss, loss of appetite
- Changes in taste
- Redness, pain or peeling of palms and soles
- High blood pressure which may cause headaches, dizziness, blurred vision

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving XL184 (cabozantinib), from 4 to 20 may have:

- Anemia which may require blood transfusion
- Pain
- Constipation, heartburn
- Dry mouth, skin
- Sores in the mouth which may cause difficulty swallowing
- Swelling of arms, legs
- Infection
- Bruising, bleeding
- Dehydration
- Muscle weakness
- Dizziness, headache
- Cough, shortness of breath
- Internal bleeding which may cause black tarry stool, blood in vomit, coughing up blood, or blood in urine
- Bleeding from multiple sites including the nose
- Changes in voice
- Hair loss, rash
- Change in hair color
- Blood clot which may cause swelling, pain, shortness of breath

RARE, AND SERIOUS

In 100 people receiving XL184 (cabozantinib), 3 or fewer may have:

- A tear or hole in internal organs that may require surgery
- Non-healing surgical site
- Damage to the jawbone which may cause loss of teeth
- Bleeding in the brain which may cause confusion
- Stroke which may cause paralysis, weakness
- Brain damage which may cause headache, seizure, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome)
- Lung collapse

Additional Drug Risks

The study drugs could interact with other drugs and food, especially grapefruit and high-fat foods, which can alter the drug levels in your blood. Your study doctor will give you a clinical trial wallet card that lists the study drugs you are taking. 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.

Photograph Risks

Photograph's will be taken of your lesions, some of which may include personal identifying features of you such as your face, a tattoo, *etc*. Photographs will be stored electronically under your ID number and back-up electronic storage will be kept. Only dedicated study staff and the sponsor will have access to the photographs. Appropriate measures will be taken to protect your confidentiality. However, there is a risk that this personal identifying information along with your medical information could be exposed by accident, but that risk is low. Your photos may be used in publication but only with prior removal of identifying characteristics, for example, the blacking out of your eyes. Although those photographs will be used without identifying information such as without your name, it is still possible that someone may recognize you. If this happens or your medical record is improperly disclosed to a third party, it could have deleterious effects such as impacting employment, insurance, *etc*.

What are my responsibilities in this study?

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

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

For women: Do not get pregnant or breastfeed while taking part in this study. **For men:** Do not father a baby while taking part in this study. **For all:** Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 5 months (women only) or 7 months (men only) after your last dose of study drugs.

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 nivolumab ready and giving it to you.
- your insurance co-pays and deductibles.
- the blood collection to see your CD4, CD8 blood counts and your HIV viral load before you begin study treatment, on Day 1 of Cycle 1, Day 1 of Cycle 3, Day 1 of Cycle 5, and then every 12 weeks, and when you stop study treatment.
- Electrocardiograms (EKGs) done at the start of each cycle to measure the activity of your heart

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 pregnancy for women of childbearing potential before you begin study treatment.
- The cost of the photographs of your lesions
- The costs of the optional blood collections for research.

You or your insurance provider will not have to pay for the XL184 (cabozantinib) and nivolumab while you take part in this study.

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

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

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

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

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

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

Who will see my medical information?

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

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

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

Some of these organizations are:

- The study sponsor and any company supporting the study or the study agents now or in the future. This would include any organization helping the company with the study.
- The NCI Central IRB, which is a group of people who review the research with the goal of protecting the people who take part in the study.
- The FDA and the groups it works with to review research.
- The NCI and the groups it works with to review research.

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

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

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

- You will not get reports or other information about any research that is done using your information.

Where can I get more information?

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

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

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor (*insert name of study doctor[s]*) at (*insert telephone number, and email address if appropriate*).

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

Optional studies that you can choose to take part in

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

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

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

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

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

Some of these studies may be about how genes affect health and disease. Other studies may look at how genes affect a person’s response to treatment. Genes carry information about traits that are found in you and your family. Examples of traits are the color of your eyes, having curly or

straight hair, and certain health conditions that are passed down in families. Some of the studies may lead to new products, such as drugs or tests for diseases.

Known future studies

If you choose to take part in this optional study, researchers will collect some of the tissue left over from your biopsy when you were diagnosed with cancer and blood for research on whether study treatment affects proteins that communicate between cells, the quantity and how well the cells of your immune system work, the amount of HIV-infected immune cells that are not currently producing HIV, and to see if the presence of cells from your immune system and special proteins in your original biopsy can help predict response to the study treatment.

Unknown future studies

If you choose to take part in this optional study, a sample of tissue from your previous biopsy and blood samples will be collected and stored. Storing samples for future studies is called "biobanking." The biobank is being run by the Cheng Laboratory of the Montefiore Medical Center (Albert Einstein Cancer Center) 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. This is a publicly funded study. Samples from publicly funded studies are required to be shared as broadly as possible. However, we will protect your privacy. The goal of this is to make more research possible that may improve people's health.

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

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

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

Unknown future research studies may include sequencing of all or part of your DNA. This is called genomic sequencing. Sequencing allows researchers to identify your genetic code. Changes in your genetic code may just be in your tumor tissue. These are called somatic changes. Changes may also be in your normal tissue and passed down through your family. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down. These are called germline changes.

If only tumor tissue is sequenced, we will not know if a genetic change in your tumor is also in your normal tissue. This is why sometimes both normal tissue and tumor tissue are sequenced.

This helps researchers understand if a genetic change happened only in your cancer tissue, or in your normal tissue as well.

What is involved in this optional sample collection?

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

1. About 3.5 tablespoons of blood will be collected from a vein in your arm before you begin treatment, on Day 1 of Cycle 3 and Cycle 5, and when your treatment is discontinued. A sample from the tissue that was collected at the time of your biopsy will also be sent to the biobank.
2. Your samples will be stored in the biobank. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until they are used for research or destroyed.
3. Researchers can only get samples from the biobank after their research has been approved by experts. Researchers will not be given your name or contact information.
4. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

What are the risks in this optional sample collection?

- The most common risks related to drawing blood from your arm are brief pain and maybe a bruise.
- Generally, hospitals will keep some of your tissue. This tissue may be used to help treat 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. Only your study doctor and a few study researchers will have access to the master list linking

the code numbers to names. The biobank and the genomic sequencing laboratory will receive your samples with the following information only: your sample code number; your age, race/ethnicity, and gender; your type of cancer; any previous treatments you received for your cancer; and the treatment you will receive for this current study.
2. Researchers who study your samples and information will not know who you are. They also must agree that they will not try to find out who you are. The researchers must be trained in the handling of private information. Any researcher who wants to study your stored samples and genetic information must apply and be approved to do so.
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, _____, at _____, 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, _____ at _____.

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 studies described above.

YES NO

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to learn about results from these studies.

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

Participant's signature

Date of signature

This is the end of the section about optional studies.

Use of the Photographs of your Lesions

I consent for photograph(s) to be used in medical publications without identifying information.

YES NO

I agree for my image to be used for my medical record but NOT FOR medical publication.

YES NO

I agree to use my image for medical records ONLY

YES NO

My signature agreeing to take part in the study

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

Participant's signature

Date of signature

Signature of person(s) conducting the informed consent discussion

Date of signature

Patient Study Calendar

	Before you begin taking the study drugs	XL184 (cabozantinib) alone	Cycle1 (Cycle Length = 28 Days)				Cycle 2 (Cycle Length = 28 Days)				Cycle 3+ (Cycle Length = 28 Days)				After you finish taking the study drugs
		Day -14 to Day 0	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	Week 10	Week 11	Week 12	
XL184 (cabozantinib)[A]		X	X ---------- X				X ---------- X				X---------- X				
Nivolumab[B]			X				X				X				
Pre-study procedures including Informed consent, Demographics, Medical history, and Height	X	--	----------	----------	----------	----------	----------	----------	----------	----------	----------	----------	--------		
Recoding of other medicines that you are taking	X	X											X		
Physical exam, Vital signs, and an assessment of how well you perform everyday tasks activities	X	X	X		X		X				X				X
Weight	X	X	X		X		X		X		X				X
Blood draws for complete blood count and general health status	X	X	X		X		X		X		X				X
EKG (as indicated)	X	X ----------	X ----------	----------	----------	----------	X ----------	----------	----------	----------	X ----------	----------	----------		
Side effects evaluation		X											X		X
Medical imaging scans for tumor measurements	X	Tumor measurements repeated every 8 weeks (2 cycles)													X
Photographs of your lesions	X	Additional photographs will be taken if you have a response to the study drugs													X
Blood or urine collection for pregnancy test (for women of childbearing potential)	X														
Urine tests	X	X	X				X				X				X
Test to check your Thyroid	X		X				X				X				X

Tests to check your pancreatic function	X	X	X				X				X				X
Blood collection for research purposes to check the level of immune cells and HIV	X		X								X[C]				X
Test to monitor heart function	X														
Collection of the XL184 (cabozantinib) medication diary		X	----	----X----	----------	----------	----------	----X----	----------	---------		X				X
Blood collection for research purposes (optional)	X										X[D]				X
Leftover tumor tissue from previous biopsy (optional)	X														

A: XL184 (cabozantinib): Dose as assigned. Take daily on an empty stomach (do not eat at least 2 hours before and 1 hour after each dosing).

B: Nivolumab: Dose as assigned on Day 1 of each cycle.

C: Day 1 of Cycle 3 before getting the study drugs, Day 1 of Cycle 5 before getting the study drugs, and every 12 weeks after that until your treatment is discontinued.

D: Day 1 of Cycle 3 and Day 1 of Cycle 5 before getting the study drugs.