To: CTEP Protocol and Information Office

From: Adel Mandl, MD

Date: August 1, 2025

Protocol: 10315 *A Phase 2 Study of XL184 (Cabozantinib) in Combination with Nivolumab and Ipilimumab for the Treatment of Poorly Differentiated Neuroendocrine Carcinomas*

SUMMARY OF CHANGES – Consent Form

#	Section	Comments
1.	Header	Updated Protocol Version Date.

To: CTEP Protocol and Information Office

From: Adel Mandl, MD

Date: June 3, 2025

Protocol: 10315 *A Phase 2 Study of XL184 (Cabozantinib) in Combination with Nivolumab and Ipilimumab for the Treatment of Poorly Differentiated Neuroendocrine Carcinomas*

SUMMARY OF CHANGES – Consent Form

#	Section	Comments
2.	Header	Updated Protocol Version Date.

Research Study Informed Consent Document

Study Title for Participants: Testing the combination of XL184 (cabozantinib), nivolumab, and ipilimumab for poorly differentiated neuroendocrine tumors

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Protocol 10315, A Phase II Clinical Trial of XL184 (Cabozantinib) in Combination with Nivolumab and Ipilimumab for the Treatment of Poorly Differentiated Neuroendocrine Carcinomas (NCT #TBD)

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 a poorly differentiated neuroendocrine tumor (*i.e.* neuroendocrine tumor that does not look like the normal tissue it arose from).

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 improve the number of patients whose neuroendocrine tumors do not grow or shrink by using a combination of XL184 (cabozantinib), nivolumab, and ipilimumab?

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

What is the usual approach to my neuroendocrine tumors?

The usual approach for patients who are not in a study is treatment with chemotherapy agents. All three study drugs, XL184 (cabozantinib), nivolumab, and ipilimumab, are cancer treatment medicines that have been approved by the Food and Drug Administration (FDA) to treat other types of cancers.

There are no treatments that are proven to help patients with poorly differentiated neuroendocrine carcinoma 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 get XL184 (cabozantinib), nivolumab, and ipilimumab for up to 4 cycles. The first 4 cycles are 21 days long. Starting from Cycle 5, you will receive XL184 (cabozantinib) and nivolumab, until your disease gets worse or the side effects become too severe. Cycle 5 and later cycles are 28 days long.

After you finish your study treatment, your doctor will continue to follow your condition for as long as you are alive or withdraw your consent and watch you for side effects. You will need to come in 4 weeks after the last day of study treatment. Thereafter, follow-ups are done with clinic visits or telephone conversations if you cannot come into clinic once every 3 months.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks

We want to make sure you know about a few key risks right now. We give you more information in the "What risks can I expect from taking part in this study?" section.

If you choose to take part in this study, there is a risk that the study drugs may not be as good as the usual approach for your cancer at shrinking or stabilizing your cancer.

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

- Diarrhea
- Nausea
- Rash
- Tiredness
- Vomiting
- Weight Loss

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

Benefits

The combination of XL184 (cabozantinib), nivolumab, and ipilimumab has not been studied for your kind of cancer in the past. The drugs nivolumab and ipilimumab in combination have been shown to shrink your type of cancer in a limited number of people with your cancer.

It is unlikely that the combination of XL184 (cabozantinib), nivolumab, and ipilimumab 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), 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 good and bad effects of the combination of study drugs XL184 (cabozantinib), nivolumab, and ipilimumab. These study drugs could shrink your cancer, but they could also cause side effects, which are described in the risks section below. The study doctors hope to learn if the study drugs will shrink the cancer in at least 60% of patients on this study.

All three study drugs, XL184 (cabozantinib), nivolumab, and ipilimumab, have already been approved by the FDA to treat other types of cancers.

There will be about 30 people taking part in this study.

What are the study groups?

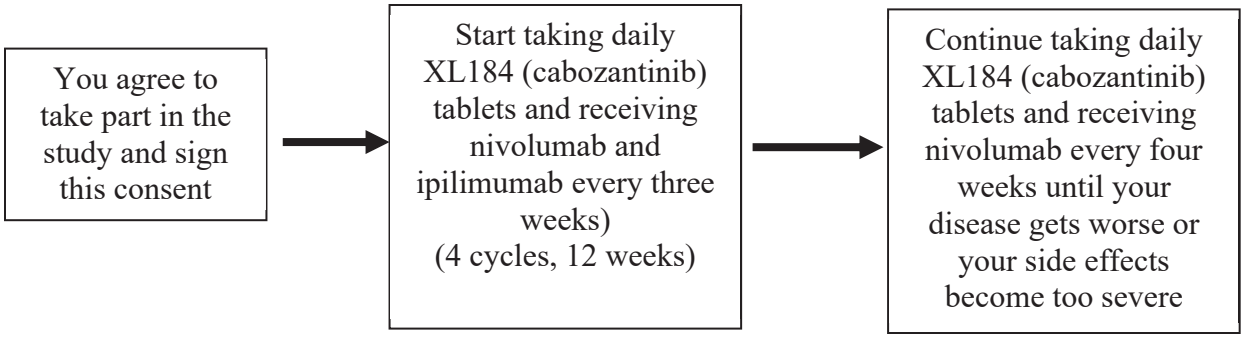
There is only one group in this study. In this study, all patients will receive the study drugs XL184 (cabozantinib), nivolumab, and ipilimumab.

Treatment schedule: You will take XL184 (cabozantinib) tablets by mouth every day for the first 4 cycles of the study. 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 due in less than 12 hours, take your next dose at the normal time. Do not make up the missed dose. You will get nivolumab and ipilimumab through a vein in your arm once every three weeks for 4 cycles. Each cycle will last 21 days (three weeks). You will receive ipilimumab for only the first four cycles (for a total of four doses). After the first four cycles, you will continue to take XL184 (cabozantinib) tablets daily and receive nivolumab once every 4 weeks until your disease gets worse or the side effects become too severe. See the study calendar for more information.

You also will keep a pill diary for XL184 (cabozantinib). This helps you keep track of when you take your pills. The study doctor will show you how to use this diary. Each time you visit the clinic, you must bring the pill diary, any remaining pills, and the pill bottle.

You will not be able to get additional doses of the drugs, other than what is outlined in the study. These drugs are not approved by the FDA for treatment of your disease.

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 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:

- Thyroid testing done every cycle.
- Pregnancy test done at the start of every cycle
- An echocardiogram at the start of the study. This is an imaging test that allows doctors to visualize the way your heart beats and shows the size, shape, and position of the heart.

This study will use genetic tests that may identify changes in the genes in your DNA. Your genes carry information about you and your family, from the color of your eyes to health conditions for which you may be at risk, such as certain kinds of cancer.

Finding these changes would not affect your treatment in this study. However, they could affect your health in other ways. If the changes in your genes were inherited, the changes could also affect the health of your family members.

You and your family may want to know about any genetic test findings that may be important to your health. You may use this form to grant us permission in advance to give this information to your doctor. If a genetic test result about you seems to be medically important and you have granted us permission to contact you, the following steps will occur:

1. Researchers will study the result further to decide if it may be medically important to you or your relatives.

2. The research laboratory that performed the genetic test will contact your doctor about the finding. The research laboratory, which will not have any identifying information about you, will provide your doctor with a code number assigned to your genetic test sample.
3. Your doctor will use the code number to identify you and will then contact you about the medically important finding. Your doctor may try to contact you several times.
4. You will require another genetic test to confirm the results. This test must be paid for at your own expense.
5. If it is confirmed that there are changes found that could cause health problems, then your doctor will discuss your options with you. We strongly suggest that you also talk to a genetic counselor. Genetic counseling services must be paid for at your own expense.

It is more likely, however, that you will not be contacted by us about a medically important finding. Even if we do not contact you, it does not mean that your genes do not contain changes that are important to your health. Researchers are always learning about new and medically important changes in genes and some information may be learned in the future. Researchers will only decide to contact you about genetic test results at the time your DNA is initially sequenced. You will not be contacted or consented for any research done using your samples in the future, and you will not receive any reports or information about any medically important findings learned in the future. Also, sometimes the meaning of genetic test results can be uncertain, and we may not know for sure what the results mean for your future health. Sharing an uncertain genetic test result with you could offer little benefit, no benefit at all, or could even be harmful.

Results from genetic testing will not be a part of your medical records, unless the results are confirmed by additional testing that you agreed to. See "Who will see my medical information?" for laws and risks in protecting your genetic information.

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 biopsies for the study. Tumor biopsies will be collected at the start of the study before you begin receiving the study drugs and during week 2 of Cycle 2. The study biopsy takes small pieces of cancer tissue from your body. This is like the biopsy you had that helped diagnose your cancer. These samples will be used to see how the study treatment affects your disease and your immune system. You and your study doctor will not get the results of this testing.
- Blood samples will also be taken for the study. The blood sample will be collected before you begin receiving study treatment. This sample will be used to compare your genes against the genetic changes in your tumor.

Researchers will obtain genetic material (DNA and RNA) from your tumor tissue and blood samples. Your DNA and RNA will be sequenced to evaluate changes in your DNA and RNA that may occur during treatment. You and your study doctor will not get any results of this testing.

A patient study calendar is attached at the end of this document. It shows how often these exams, tests, and/or 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 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 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.

Genetic Testing Risks

The genetic test used in this study will test your tumor and normal tissue to understand the composition of your cancer. Changes found in your normal tissue may be passed down in families. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down.

Genetic tests of normal tissue can reveal information about you and also about your relatives. Your doctor will talk with you about what the tests results may mean for you and your family. He or she also may suggest you talk with a genetics counselor to learn more. You or your insurance plan would have to pay for visits to a genetic counselor.

Biopsy Risks

Common side effects of a biopsy are a small amount of bleeding at the time of the procedure, bruising, and pain at the biopsy site. Pain can be treated with regular pain medications. Rarely, an infection, significant bleeding, or collapsing of the lung can occur if biopsy is taken from the lungs. You may sign a separate consent form for the study biopsy that describes the risks in more detail.

Blood Draw Risks

You may feel discomfort during some of the tests or procedures during this study or may experience some inconveniences. Some of the risks from drawing blood from your arm may include pain, bruising, lightheadedness, and rarely, infection. 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 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.

Diarrhea is a common side effect associated with XL184 (cabozantinib). 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 XL184 (Cabozantinib)
(CAEPR Version 2.5, August 29, 2024)

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
- In children or adolescents: may interfere with growth
- 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

Possible Side Effects of Nivolumab
(Table Version Date: December 2, 2020)

Special precautions
Side effects of Nivolumab may happen anytime during treatment or even after your treatment has ended. Some of these problems may happen more often when Nivolumab is used in combination with ipilimumab. **Call or see your healthcare provider right away**

if you develop any problems listed below or the symptoms get worse.

COMMON, SOME MAY BE SERIOUS

In 100 people receiving Nivolumab, more than 20 and up to 100 may have:

- Tiredness

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving Nivolumab, from 4 to 20 may have:

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

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

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

RARE, AND SERIOUS

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

- Dry eyes
- Sores in the mouth which may cause difficulty swallowing
- A syndrome starting with flu-like symptoms and followed by swelling, tenderness

which may cause blurred vision, ringing in the ears, changes in hair or hair loss
- Swelling of the bowels

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

Possible Side Effects of Ipilimumab
(Table Version Date: March 29, 2019)

Special precautions

Side effects of ipilimumab (MDX-010) may happen anytime during treatment or even after your treatment has ended. Some of these problems may happen more often when ipilimumab (MDX-010) is used in combination with BMS-936558 (nivolumab). **Call or see your healthcare provider right away if you develop any problems listed below or the symptoms get worse.**

COMMON, SOME MAY BE SERIOUS
In 100 people receiving ipilimumab (MDX-010), more than 20 and up to 100 may have:

- Diarrhea, nausea

- Tiredness

Ipilimumab (MDX-010) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Skin: itching; rash, blisters including inside the mouth (can be severe); hives

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

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

Ipilimumab (MDX-010) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Lung problems (pneumonitis). Symptoms may include: new or worsening cough, chest pain, shortness of breath
- Intestinal problems (colitis) that can rarely lead to tears or holes in your intestine. Signs and symptoms of colitis may include: diarrhea or increase in bowel movements, blood in your stools or dark, tarry, sticky stools, severe belly pain or tenderness
- Kidney problems, including nephritis and kidney failure requiring dialysis. Signs of kidney problems may include: decrease in the amount of urine, blood in your urine, ankle swelling.
- Problem of the muscle, including inflammation, which can cause muscle pain and severe muscle weakness sometimes with dark urine
- Problem of the nerves that can cause paralysis. Signs and symptoms may include: numbness, tingling of hands and feet; weakness of the arms, legs and facial muscle movement.
- Liver problems (hepatitis) which can cause liver failure. Signs and symptoms of hepatitis may include: yellowing of your skin or the whites of your eyes, severe nausea or vomiting; drowsiness; pain in the right upper belly
- Hormone gland problems (especially the thyroid, pituitary and adrenal glands, and pancreas). Signs and symptoms may include: headaches that will not go away or

unusual headaches, extreme tiredness or changes in mood or behavior decreased sex drive; weight loss or weight gain; excessive thirst or urine; dizziness or fainting.

RARE, AND SERIOUS In 100 people receiving ipilimumab (MDX-010), 3 or fewer may have:
• Bleeding • Blockage of the bowels which may cause constipation • Fluid around heart • Severe illness with multiorgan failure • Confusion Ipilimumab (MDX-010) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to: • A condition with high blood sugar which leads to tiredness, frequent urination, excessive thirst, headache, nausea and vomiting, and can result in coma • Heart problems including inflammation and heart failure. Symptoms and signs of heart problem may include: Shortness of breath, swelling of the ankle and body • Complications associated with stem cell transplant using donor stem cells (allogeneic stem cell transplant). These complications are caused by attack of donor cells on the host organs (inducing liver, skin and gut), and can lead to death. If you are considering an allogeneic stem transplant after participating in this study, please tell your doctor that you have received ipilimumab therapy, since the risk and severity of transplant-associated complications may be increased. • Swelling of the brain (meningitis/encephalitis), which may cause: headache, confusion, sleepiness, seizures, and stiff neck

Additional Drug Risks

The study drug could interact with other drugs. 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.

Do not take grape/fruit juice while taking XL184 (cabozantinib). Check with your study doctor before taking any over-the-counter products or herbal medicines like St. John Wort's.

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 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 cost of getting the study drugs ready and giving them 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 EKGs in this study done at every treatment cycle.
- The biopsy for testing molecular composition of your tumor at the beginning of the study and during week 2 of the second cycle of treatment.
- The blood test at the beginning of the study to look at genetic changes in your tumor.

You or your insurance provider will not have to pay for the XL184 (cabozantinib), nivolumab, and ipilimumab 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.
- The NCI's National Clinical Trials Network and the groups it works with to conduct 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.

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, 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*).

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.

Participant's signature

Date of signature

Signature of person(s) conducting the informed consent discussion

Date of signature

Attachment A: Study Calendar for Protocol 10315 Consent Form

	Pre-study	Cycles 1 – 4 (Cycle length = 3 weeks)												Cycles 5+: Cycle length = 4 weeks	When your disease gets worse of the side effects become too severe	4 weeks after last dose of study drug	Long term follow-up off study treatment
		Cycle 1			Cycle 2			Cycle 3			Cycle 4			Cycle 5+			
		Week 1	Week 2	Week 3	Week 1	Week 2	Week 3	Week 1	Week 2	Week 3	Week 1	Week 2	Week 3	Day 1			
XL184 (cabozantinib)[A]		X———												X			
Nivolumab[B]		X			X			X			X			X			
Ipilimumab[C]		X			X			X			X						
Classification of how much or how little tumor tissue looks like the normal tissue it came from	X																
Pre-study procedures including Informed consent, Demographics, Medical history, and Height	X																
Concurrent meds	X	X———												X			
Physical exam, Vital signs, Weight, Performance status	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[E]	
Urine tests	X	X			X			X			X			X	X	X[E]	
Blood or urine collection for pregnancy test	X	X			X			X			X			X			
Thyroid tests	X	X			X			X			X			X	X	X[E]	
Assessment of your heart history, heart muscle, and size, shape, and position of the heart (*i.e.* echocardiogram) [After Pre-Study, the assessments will be taken as your doctor indicates it is necessary]	X																

	Pre-study	Cycles 1 – 4 (Cycle length = 3 weeks)												Cycles 5+: Cycle length = 4 weeks	When your disease gets worse of the side effects become too severe	4 weeks after last dose of study drug	Long term follow-up off study treatment
		Cycle 1			Cycle 2			Cycle 3			Cycle 4			Cycle 5+			
		Week 1	Week 2	Week 3	Week 1	Week 2	Week 3	Week 1	Week 2	Week 3	Week 1	Week 2	Week 3	Day 1			
EKG[D]	X	X			X			X			X			X	X	X[E]	
Side effects evaluation		X→														→X	
Medical imaging scans for tumor measurements	X							X						Tumor measurements are repeated every 2 cycles for the first 6 months and every 3 cycles thereafter	X	X	
Tumor Biopsy for research purposes	X					X											
Blood collection for research purposes	X																
Follow-up (the assessment will be taken as your doctor indicates it is necessary)																	X

A: XL184 (cabozantinib): Dose as assigned.

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

C: Ipilimumab: Dose as assigned on Day 1 of Cycles 1-4 (total of four doses).

D: EKG will be performed at baseline, on Day 1 of Cycles 1 to 5, and then every 8 weeks (every other cycle).

E: At 4 weeks after the last dose of the study drugs, these assessments will be repeated if your doctor thinks it is necessary.