The Ohio State University Combined Consent to Participate in Research and HIPAA Research Authorization

Study Title:	**Phase II study of ponatinib for advanced cancers with genomic alterations in fibroblastic growth factor receptor (FGFR) and other genomic targets (KIT, PDGFRα, RET FLT3, ABL1)**
Principal Investigator:	**Sameek Roychowdhury, MD, PhD**
Sponsor:	**OSU**
Funding Sponsors:	National Institutes of Health (NIH) and Takeda Pharmaceutical Company

- **This is a consent form for research participation.** It contains important information about this study and what to expect if you decide to participate. Please consider the information carefully. Feel free to discuss the study with your friends and family and to ask questions before making your decision whether or not to participate.
- **Your participation is voluntary.** You may refuse to participate in this study. If you decide to take part in the study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your usual benefits. Your decision will not affect your future relationship with The Ohio State University. If you are a student or employee at Ohio State, your decision will not affect your grades or employment status.
- **You may or may not benefit as a result of participating in this study.** Also, as explained below, your participation may result in unintended or harmful effects for you that may be minor or may be serious depending on the nature of the research.
- **You will be provided with any new information that develops during the study that may affect your decision whether or not to continue to participate.** If you decide to participate, you will be asked to sign this form and will receive a copy of the form. You are being asked to consider participating in this study for the reasons explained below.

1. Why is this study being done?

The purpose of this study is to find out what effects; good and/or bad, ponatinib has on you and your cancer. Your body has proteins that are involved in a cancer's ability to grow and survive. Ponatinib may prevent these proteins from causing cancer growth.

To enter the study, you must have genetic testing performed on your cancer. The testing will determine which cancer genes are altered in your cancer and may be targeted by the study drug ponatinib.

The genetic testing being used to decide if you qualify for this study is not an FDA (Food and Drug Administration) approved test; therefore its accuracy in identifying you as a candidate for this trial is unknown and there is a possibility you may not benefit from ponatinib.

Ponatinib has been approved by the FDA for use in blood cancers for whom no other therapy with similar drugs is indicated. Ponatinib has not been approved for use in other cancers. Therefore, this study will evaluate whether Ponatinib is effective in other types of cancers such as yours.

2. How many people will take part in this study?

About 45 people will take part in this study with approximately 25 people participating at The Ohio State University Wexner Medical Center.

3. What will happen if I take part in this study?

Before you begin the study …

You will need to have the following exams, tests or procedures to find out if you can be in the study. Some of these exams, tests or procedures are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- You will need to supply a complete list of your current medications to the study doctor. This includes over-the-counter medications and herbal supplements. Some medications may interact adversely with ponatinib and it is important that your study doctor and prescribing physician be aware of any potential risks so that they can prescribe alternative medications as necessary.
- The study team will ask you questions about your demographics (examples are sex, race, age, height, weight, etc.) and your medical history
- The study team will ask what medications you are currently taking
- Physical exam
- Vital signs (including blood pressure, temperature and pulse)
- The study team will ask you how you are currently feeling and your ability to do your daily tasks (performance status)
- Routine blood tests (serum chemistry and CBC - complete blood count)
- Additional blood tests (serum lipase, a fat digesting enzyme)
- EKG (Electrocardiogram) a line graph that shows changes in the electrical activity of the heart over time.
- Eye exam
- A urine pregnancy test if you are a woman
- Tests to measure your tumor. This could be any of the following tests:
    - Clinical measurement of superficial lesions – these will be done with a ruler or tape measure to measure the lesion on the skin. This will be done in patients who have lesions that can be measured by physical exam
    - CT – a series of detailed pictures of areas inside the body. The pictures are taken from different angles.
    - MRI – a procedure in which radio waves and a powerful magnet linked to a computer is used to make detailed pictures of inside the body.

  - PET scan is a procedure in which a small amount of radioactive imaging agent is injected into a vein. Then a scanner is used to make detailed pictures of areas inside the body where the sugar is used. A PET-CT scan is a type of scan which uses a combination of PET and CT scanning.
  - Ultrasound is a procedure in which high-energy sound waves are bounced off internal tissue or organs and make echoes. The echo patterns are shown on the screen of an ultrasound machine, forming a picture of body tissues.
- Either an echocardiogram or a MUGA scan (measures your heart's ability to pump) to assess the strength of your heart
- Genetic testing of your cancer is required to enter the study. If it has not been previously tested, then you will need to have genetic testing of your cancer. You will be asked to sign a separate consent form for Precision Cancer Medicine in order for researchers to perform genetic testing on blood and tissue samples. The study doctor will discuss this additional portion of the study with you, if your genetic testing has not previously been performed on your tissue.
- A tumor biopsy or a previously collected tumor biopsy sample will be collected, as described in the bullet-point above, for research purposes and is required for this study. This will be used to study your cancer in relation to the study drug ponatinib. If your samples have already been collected for Precision Cancer Medicine, you will not need to complete the testing again before entering this study.

During the study…
You will not need to be hospitalized to take part in this study unless you experience a serious side effect.

Ponatinib should be taken by mouth daily with or without food. Tablets should be swallowed whole. Do not crush or dissolve the tablets.

You will be required to take **aspirin** (81 or 325 mg daily) for the duration of ponatinib treatment to protect against blood clots.

Some of the following exams, tests, and procedures may be completed via Telehealth visit (phone, video call, or email) if the investigator deems it appropriate. Ask your physician if you have quetsions about Teleheath or Telehealth visits.

If the exams, tests and procedures show that you can be in the study, and you choose to take part, then you will need the following tests and procedures. They are part of regular cancer care.

- The study team will also ask you how you are currently feeling and your ability to do your daily tasks.
- Routine physical exam, which will include measurement of your tumor with a ruler or tape if it is measurable by physical exam.
- Routine vital signs – pulse, blood pressure, temperature
- Weight

- Routine blood tests will be performed at the beginning of every cycle which will be every 28 days. Some blood tests would be repeated every 2 weeks for the first two cycles.
- Routine scans to look for a response to treatment will be done every 2 cycles. This will be a CT scan most commonly, but may also include a bone scan, an MRI, or a PET-CT scan (more often if your doctor tells you to).

You will need these tests and procedures that are part of regular cancer care. They are being done more often because you are in this study.

- The study team will ask you what medications you are currently taking, if you are having any side-effects.
- Blood tests would be performed every 2 weeks for the first 2 cycles and every cycle after that (or more often if your doctor feels it is necessary).
- EKG may be obtained if your doctor feels it is necessary.
- Either an echocardiogram or a MUGA scan may be obtained if your doctor feels it is necessary.

You will need these tests and procedures that are either being tested in this study or being done to see how the study is affecting your body.

- You will take your blood pressure twice per week at home using a blood pressure cuff. The cuff will be provided by Takeda. You will be given a medication diary on which you will also record your blood pressure readings. Blood pressure will be monitored at home, because high blood pressure or hypertension may require treatment with medication to prevent further complications.
    - **If any reading is greater than or equal to 160/90, you must contact the study team using the phone number in Section 14.**
    - You will need to come into clinic where the study staff will measure your blood pressure again to confirm the reading. If you develop high blood pressure or hypertension during the study, the study doctor may prescribe medication, reduce your dose of ponatinib, or stop it altogether.
- You will be asked to maintain a medication diary documenting when you take the therapy and must bring it to each visit with your physician.
- Please check with your doctor/prescriber or pharmacist before using any new over-the-counter medications or herbal supplements.
- A mandatory second tumor biopsy sample may be performed for research purposes after completion of ponatinib, if your disease progresses. This will be used to study why your cancer was resistant to ponatinib and will also be used to test for any new gene alterations that might make you eligible to consider participating in another Precision Cancer Study with a different drug. This will only be performed if your treating physician considers it safe for you to complete.
- Research specimens from the Precision Cancer Study will be shared with this study, in order to facilitate your eligibility, enrollment, and further our understanding of cancer.

- Characterization of your cancer in relation to ponatinib will be performed to better understand which patients may benefit from ponatinib therapy. This study will work closely with another study at Ohio State University, the Precision Cancer Study, to facilitate this research.

When I am finished taking ponatinib…

You will need the following tests and procedures, part of regular cancer care.

- The study team will also ask you how you are currently feeling and your ability to do your daily tasks.
- The study team will ask you what medications you are currently taking, if you are having any side-effects.
- Physical Exam, which will include measurement of your tumor with a ruler or tape if it is measurable by physical exam.
- Vital signs – pulse, blood pressure, temperature
- Weight

4. How long will I be in the study?

You can stay on this study until one of the following happens:

- Your cancer gets worse,
- You get sick and cannot stay on this study,
- You have unacceptable side-effects,
- You decide to stop being on this study,
- Your study doctor thinks it is best for you not to be on this study any more.

After you stop this study, you will be followed for 52 weeks or until death, whichever occurs first. If you stop this study because of a side-effect, you will be followed until the side effect gets better or is stabilized.

5. Can I stop being in the study?

You may leave the study at any time. If you decide to stop participating in the study, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. Your decision will not affect your future relationship with The Ohio State University.

It is important to tell the study doctor if you are thinking about stopping so any risks from ponatinib can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best health interest; if you do not follow the study rules; or if the study is stopped.

If you decide to withdraw from the study, or if you are withdrawn, additional data will not be collected from you. Information that has already been collected for the research cannot be withdrawn. Any specimens that were previously collected from you cannot be withdrawn from the research.

6. What risks, side effects or discomforts can I expect from being in the study?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking ponatinib. *In some cases, side effects can be serious, long lasting, or may never go away. There also is a risk of death.*

It is very important that you report any side effects (also referred to as "adverse events") to your study doctor as soon as possible.

The following are the most rare and serious risks of ponatinib.

- Vascular Occlusion (or blockage of a blood vessel)
  Blood clots or bloackages in your arteries of veins (blood vessels) or narrowing in your arteries can occur in your heart, brain, and legs and may lead to:
  - heart attack
  - stroke

  These risks may lead toamputation, or death. They may require medical treatment, or urgent medical attention, possibly including surgery to re-open or "bypass" the blocked arteries or veins.

  Blood clots or narrowing of the arteries in your arms or legs can cause pain or swelling, which may require urgent medical attention, including blood-thinning medication, surgery to re-open or bypass the arteries or vein, or amputation.

  Blood clots or narrowing of the arteries can occur in the lungs (causing fluid buildup in the lungs, eyes (which may lead to difficulty seeing or loss of sight), or other organs.

  These events have occurred in clinical studies, with humans, throughout the treatment period, both early on and even after 2 or 3 years of treatment. They were more frequent in older patients and in those with preexisting conditions, such as poor blood flow to organs, high blood pressure, diabetes, or high cholesterol. However, these events have been experienced by patients both older and younger than 50, and those with and without pre-existing conditions.

  Seek immediate medical attention if you experience symptoms suggesting:
  - A heart attack, such as:

  - Chest pain or pressure
  - Pain in your arms, back, neck or jaw, or shortness of breath
- A stroke, such as:
  - Numbness or weakness on one side of the body
  - Trouble talking
  - Severe headache
  - Dizziness
- Blood clots in a vein, such as:
  - Pain or swelling in an arm or leg
- Artery blockage or narrowing in an arm or leg, such as:
  - Cold, discolored, painful arm, leg, hand, foot, fingers, or toes

- Heart Failure
  Heart failure is a condition in which the heart does not pump enough blood to the rest of the body. It can cause fatigue, shortness of breath, and swelling of the legs. It can lead to death. Seek medical attention right away if you experience any of the following symptoms:
  - Difficulty breathing
  - Chest pain
  - Fast or irregular heartbeats
  - Dizziness
  - Feeling faint

- High Blood Pressure
  Elevations in your blood pressure could occur, with the potential to become serious and lead to hospitalization. Contact the study doctor if you have symptoms of high blood pressure, including:
  - Headache
  - Dizziness
  - Chest pain
  - Difficulty breathing

- Liver Problems
  Problems, including liver failure or blood markers suggesting your liver may not be working well, which can be severe and may lead to death. Your study doctor will do blood tests before and during your treatment with ponatinib to check for liver problems. Get medical help right away if you have any of these symptoms of liver problems during treatment:
  - Yellowing of your skin of the white part of your eyes (jaundice)
  - Dark “tea-colored” urine
  - Sleepiness

Hepatitis B (HBV) reactivation is an abrupt increase in HBV in a patient with inactive or past HBV. HBV reactivation can lead to elevations in liver enzymes, and in some cases the development of acute liver failure, and even death. People who have previously had HBV are at an increased risk of reactivation when treated with a TKI,

like the study drug. An HBV test will be done to determine whether or not you are at risk for HBV reactivation. You may need to be treated with an antiviral if you test positive for HBV, depending on your risk category and/or symptoms.

- Inflammation of your Pancreas (Pancreatitis)
  Ponatinib is associated with pancreatitis, an inflammation of the pancrease (an organ in the abdomen which produces insulin and certain digestive enzymes. They are released into the blood when the pancreas is diseased or inflamed. Inflammation of the pancreas can affect it's ability to function and can cause pain in the abdomen (belly), which can be severe and increase blood sugar levels. Pancreatitis most commonly occurs during the first 2 months of treatment.

- Low Blood Cell Counts
  Ponatinib may cause low platelets in your blood cell counts . With low platelets, this may increase your risk of bleeding. Your study doctor will check your blood counts regularly during treatment with ponatinib. Tell the study doctor right away if you experience excess bruising, nose bleeds, or other types of bleeding.

  Ponatinib may cause low neutrophils in your blood, called neutropenia.These are white blood cells that help your body fight off infection. If you experience neutopenia, you will be greater risk of developing an infection.

  If platelets and red and white blood cells are decreased , you may experience increased risk of infection, easy bruising, fatigue, shortness of breath, weakness, and bleeding.

- Bleeding
  Bleeding can be serious and if uncontrolled, may lead to death. You must tell the study doctor if you have unusual bleeding or bruising.

- Tumor Lysis Syndrome
  Patients with ALL are at increased risk of Tumor lysis syndrome (TLS) with cytotoxic/cytolytic therapy. In patients with ALL, those with white blood cell (WBC) count ≥100,000 are considered high risk. In TLS, the dying tumor cells release their contents into the blood which can cause changes to important blood chemicals and may cause damage to organs including the kidneys, heart and liver. Before starting ponatinib, your doctor will ensure that you are hydrated and may check levels of uric acid in your blood to reduce the risk of TLS developing. You will be monitored throughout the study for any signs or symptoms of TLS. If you develop TLS, your doctor will decide on your treatment, which may include intravenous hydration, dialysis, or medications to normalize the levels of your blood chemicals.

Common Side Effects:

- An upper respiratory infection, like the common cold
- Low blood platelet counts (which may increase the risk of bleeding)

- Skin rash (reddened skin or red rash with or without raised bumps, may be itchy, dry with flaking or peeling skin, less commonly may resemble acne)
- Dry skin
- Pain in the belly (abdominal pain)
- Constipation
- Nausea
- Headache
- Low blood counts including white blood cells (which may increase the risk of infection) or red blood cells (which can cause you to feel tired or short of breath)
- Shortness of breath
- Cough
- Vomiting
- Diarrhea
- Fever
- Decreased appetite
- Trouble getting amounts of, or quality of, sleep
- Dizziness
- Weakness
- Increased lipase level (an enzyme measured in the blood that reflects function of the pancreas. Elevations in lipase may indicate inflammation of the pancreas)
- Increased enzymes from the liver in the blood, alanine aminotransferase (ALT) and aspartate aminotransferase (AST)
- Pain that may occur in the joints, muscles, bones, back, or limbs
- Muscle cramps and pain
- Fatigue
- High blood pressure (hypertension)

Uncommon Side Effects:

- Pneumonia (an inflammation of the lung, generally caused by infection, that may be accompanied by cough, phlegm, fever, sharp chest pain, skaing, chills, sweating, difficulty breathing, and requires immediate medical attention)
- Stomach acid, or bile in your digestive system, may occasionally flow back up (reflux) into your food pipe (esophagus), which can cause heartburn
- Lack of energy, or lack of interest in doing things you usually do
- Neck pain
- Muscle pain caused by too little flow of blood during walking or exercise
- Confusional state (delirium) is a state that causes your mind to be unclear
- Inflammation of the pancreas (an organ in the abdomen which produces insulin and certain digestive enzymes) which may affect the function of the pancreas and which may cause pain in the abdomen (belly) which can be severe and may increase blood sugar
- Irregular heart rhythms including atrial fibrillation (an abnormal rapid or irregular heart rhythm which may cause light-headedness, shortness of breath or weakness) and abnormally rapid or slow heart rates

- Increased pressure of the blood vessels in your lungs, which can cause symptoms such as shortness of breath during routine activity (for example, climbing two flights of stairs), tiredness, chest pain, and a racing heartbeat.
- Chest pain not due to heart disease
- Chills
- Skin problems that may include rash, be itchy or painful with dry, flaking, and/or peeling skin, sometimes over a large area of your body (dermatitis exfoliative). This may include bruising, redness, change or loss of skin color due to bleeding below the skin surface, or darkening or thickening of the outer layer of skin
- Dry mouth
- Hot flush (a feeling of warmth that spreads over the body most strongly felt in the head and neck region)
- Hair loss
- Bloating
- Abdominal discomfort
- Weight decreased
- Excessive sweating sometimes during sleep
- Bleeding such as nosebleeds or petechiae (in which tiny purple or red dots appear on the skin due to bleeding under the skin's surface) or other more severe bleeding
- A rash with spots that may look like a target (erythema multiforme)
- Low levels of important electrolyte levels in your blood including abnormally low levels of potassium (which can cause irregular heartbeats), low levels of calcium (which can cause muscle spasms, twitches or cramps or numbness/tingling in your fingers, toes and around your mouth), and low levels of phosphorus (which can cause bone pain, confusion, muscle weakness)
- Increased enzymes moving from the liver into the blood, called alkaline phosphatase (ALP) and glutamyltransferase (GGT)
- High blood sugar levels
- Increased triglyceride and cholesterol levels (blood fat)
- High concentration of uric acid in the blood which could result in inflammation of a joint ("gout"), problems with urination or kidney stone, fever, chills, fatigue
- An increase in the blood of a substance produced by the liver (bilirubin) that could indicate liver disease and in high amounts can cause yellowing of the skin and eyes
- Indigestion or upset stomach
- Feeling sick or discomfort
- Voice impairment such as hoarseness
- Febrile neutropenia (a condition marked by fever and lower-than-normal number of a certain kind of white blood cell in the blood which could increase the risk of infection)
- Flu like symptoms, which can include fever, chills, body aches, nausea, loss of appetite
- Cranial or peripheral neuropathy, conditions in which nerves that come from the brain (cranial nerves), supplying the face and eyes, and nerve that come from the spinal cord (peripheral nerves) have been damaged. This can cause visual disturbances, weakness, face droop, numbness, tingling, prickling sensation, and either decreased or increased sensitivity of the skin to touch or pain, or the ear to sound.

- Inflammation or infection of one or more hair follicles. A hair follicle is an opening in the skin that encloses a strand of hair from which the hair grows
- Dehydration
- Impotence (inability to achieve or maintain an erection long enough to engage in sexual intercourse)
- A severe infection in the body, sometimes known as blood poisoning, which can cause difficulty breathing, coagulation of the blood, malfunction of your organs and is usually treated in an intensive care unit of a hospital
- Migraine headache
- Inflammation of the mucous lining of any of the structures in the mouth, including cheeks, gums, tongue, lips, throat and roof or floor of the mouth
- Eye problems can occur, including dry eye, blurred vision, eye irritation or pain, redness of the eye, eyelid swelling. Less frequently, inflammation or an ulcer of the cornea can occur. The cornea is the clear, dome-shaped tissue on the front of your eye that covers the pupil and iris.
- Narrowing of blood vessels that restricts flow to areas away from the center of the body, such as legs, arms, toes, fingers, ear lobes, and penis.
- Pericardial effusion (an abnormal buildup of fluid inside the sac that surrounds the heart which may cause chest pain, difficulty breathing, fever)
- Pleural effusion (an abnormal buildup of fluid around the lungs which may cause chest pain, cough, or shortness of breath)

Rare Side Effects:

- Bleeding that can be serious and can lead to death including bleeding in the brain or in the gastrointestinal tract (which extends from the mouth to the anus)
- Shortness of breath
- Abnormal buildup of fluid which may cause swelling in the hands, feet, ankles, face, or all over the body
- Itching of the skin
- Hypersensitivity
- Sudden, severe increase in blood pressure occurring in individuals who have untreated high blood pressure or have stopped taking antihypertensive medication
- Erythema nodosum (an inflammation of the fat cells under the skin that causes tender lesions on the skin)
- Formation of an abnormal connection between internal organs in the belly that are not normally connected
- A condition that occurs after the start of anti-cancer treatment in which the dying tumor cells release their contents into the blood. This causes changes to important blood chemicals and may cause damage to organs including the kidneys, heart, and liver.

- Poor peripheral circulation is a condition in which the blood vessels cannot supply enough blood to your feet or legs. You could experience numbness and cramping in the feet or lower legs, or experience a tingling sensation in the feet and toes.
- Splenic infarction, a condition in which oxygen supply to the spleen is interrupted, leading to partial or complete infarction (tissue death due to oxygen storage) in the spleen
- QT Prolongation, a change in heart rhythm detected on an electrocardiogram (ECG) that may be associated with sudden death
- Impaired wound healing
- Development of a hole in the esophagus, stomach, or intestines, which may be associated with pain, infection, or bleeding, and may require surgery to repair it.
- Blood vessels inside your skull becoming blocked by a blood clot, which is one of the causes of stroke
- Blood vessels inside your eyes becoming blocked by a blood clot, which may cause severe damage to your eyes. It may cause you to not be able to see clearly or could even cause blindness
- Splenic infarction, a condition in which oxygen supply to the spleen is interrupted, leading to partial or complete infarction (tissue death due to oxygen shortage) in the spleen
- Narrowing of arteries that carry blood to one or both of the kidneys
- Cerebrovascular accident, commonly known as a stroke, in which some of the brain tissue is damaged by a disruption of blood flow to the brain and may cause sudden weakness or numbness on one side of the body, and difficulty speaking which requires immediate medical attention
- Cerebral infarction, an area of brain tissue damaged by a disruption of blood to the brain, which may be associated with stroke
- Transient ischemic attacks, commonly known as a TIA or mini stroke, a TIA is an episode in which blood flow to the brain is temporarily reduced which may cause temporary sudden weakness or numbness on one side of the body, difficulty speaking and requires immediate medical attention
- Myocardial infarction, commonly known as heart attack, is an episode in which some of the heart's blood supply is severely cut off or restricted due to severe narrowing or blockage of arteries in the heart, causing the heart muscle to be damaged due to lack of oxygen
- Pain, discomfort or pressure in the chest caused by insufficient blood supply to the heart muscle
- Blood clot in blocking the major veins in the legs, pelvis, or elsewhere
- Obstruction of a blood vessel in the lungs resulting in fluid build-up in the lungs and affecting the respiratory functions (breathing)

- Increased pressure of the blood vessels in your lung, which causes symptoms such as shortness of breath during routine activity (for example, climbing two flights of stairs), tiredness, chest pain
- Hypothyroidism (less active thyroid gland)
- Heart failure, a chronic condition in which the heart does not pump blood as well as it should

Additionally, some discomforts and risks that occur with lesser frequency (<1%) than those previously mentioned should be noted because they are severe, life-threatening or fatal and may involve:

- Rash
- Blistering
- Skin peeling and mouth sores, including erythema
- Multiforme and Stevens Johnson syndrome have also been reported in some patients taking ponatinib. These rashes are disorders of the immune system, which differ from regular skin rashes and are generally more severe.

Unexpected Side Effects

Ponatinib may cause side effects that we cannot know ahead of time, some of which could be serious or even cause death in rare circumstances. Also, allergic reactions could happen in some people. Ponatinib may interfere with other drugs you need, or other drugs you take may interfere with ponatinib.

You should tell the study doctor about any changes in your health that develop while you are in this study, even if you don't think they are related to the study.

Reproductive and Pregnancy Risks

Information for women:

There is not enough medical information to know about the effects of ponatinib on an unborn child. Ponatinib may cause harm to your unborn baby. It is also not yet known if ponatinib passes into breast milk, or if it will harm a nursing infant. You should not become pregnant or breastfeed while taking ponatinib. Tell the study doctor right away if you become pregnant, think you may be pregnant, or plan to become pregnant.

You will be required to take a pregnancy test at the Screening Visit to ensure you are not pregnant before entering the trial. You are required to use a reliable method of birth control during study dosing and at least 4 months after your last dose of study drug. If you become pregnant while you are on this trial, or within 4 months of your last dose of study drug, you must tell the study doctor. The study doctor may remove you from the trial. You will be asked for your consent for researchers to collect information about the health of your baby.

Acceptable methods of contraception for women:

- Any form of hormonal contraception (birth control pills or intra-uterine devices, IUD)
- Condom or diaphragm with spermicide

Information for men:
You are required to use a reliable method of birth control during trial dosing and until at least 4 months after your last dose of study drug. If your partner becomes pregnant while you are on this trial, or at least four months after your last dose of study drug, you must tell the study doctor. You and your partner will be asked for your consent for researchers to collect information about the mother's health and that of the baby.

Medications to Avoid:
Herbal medications, such as St. John's Wort, Blue Cohash, and Estroven, must not be taken for 2 weeks prior to the first dose of study drug and for as long as you continue taking the study drug. **You must tell the study doctor about all drugs and supplements you are taking while in this study.**

Biopsy: The risk of a biopsy can include bleeding, pain, and infection. To reduce these risks, the site of the biopsy will be numbed and sterile techniques will be used. Your doctor will discuss the safest method and location to perform the biopsy.

Blood draws: A blood draw may cause faintness, inflammation of the vein, pain, bruising, or bleeding at the site of puncture. There is also a slight chance of infection. The blood samples will be taken by individual needle sticks into one of your arm veins or, if necessary, by an indwelling catheter (a thin plastic tube placed in a vein in your arm).

Genetic Research Risks: This research involves genetic studies and information. Although procedures have been put into place that are designed to make it very difficult for the results from genetic research to be linked to you, there is a remote possibility that information from your participation in this study could adversely affect you or your family in some way if a genetic disorder were discovered.

7. What benefits can I expect from being in the study?

Taking part in this study may or may not make your health better. While doctors hope that **ponatinib** will be more beneficial against your cancer compared to the usual treatment, there is no proof of this yet. We do know that the information from this study will help doctors learn more about ponatinib as a treatment for cancer. This information could help future cancer patients.

8. What other choices do I have if I do not take part in the study?

You may choose not to participate without penalty or loss of benefits to which you are otherwise entitled.
Your other choices may include:

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting no treatment

- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Talk to your doctor about your choices before you decide if you will take part in this study.

9. What are the costs of taking part in this study?

Study drug ponatinib will be provided by the Takeda Pharmaceutical Company at no cost to you. You and / or your insurance company will not be charged for the cost of any tests or procedures that are required as part of the research study and are outside the standard of care (what is normally done) for your condition.

You and / or your insurance company will be responsible for the cost of routine medications, tests and procedures that you would receive even if you were not in this research study. You and / or your insurance company will be responsible for any co-payments, co-insurance and deductibles that are standard for your insurance coverage.

Participating in this research study may lead to additional costs to you. In some cases, it is possible that your insurance company will not pay for these costs because you are taking part in a research study. Before deciding to be in this research study you should check with your insurance company to find out what they will pay for.

The National Institutes of Health is providing funding to The Ohio State University for this study. The MUGA scan or echocardiogram will be paid for by the research study. The research study will also pay for the mandatory second biopsy if your disease progresses.

10. Will I be paid for taking part in this study?

You will not be paid for taking part in this study.

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

If you suffer an injury from participating in this study, you should notify the researcher or study doctor immediately, who will determine if you should obtain medical treatment at The Ohio State University Medical Center.

The cost for this treatment will be billed to you or your medical or hospital insurance. The Ohio State University has no funds set aside for the payment of health care expenses for this study.

12. What are my rights if I take part in this study?

If you choose to participate in the study, you may discontinue participation at any time without penalty or loss of benefits. By signing this form, you do not give up any personal legal rights you may have as a participant in this study.

You will be provided with any new information that develops during the course of the research that may affect your decision whether or not to continue participation in the study.

You may refuse to participate in this study without penalty or loss of benefits to which you are otherwise entitled.

An Institutional Review Board responsible for human subjects research at The Ohio State University reviewed this research project and found it to be acceptable, according to applicable state and federal regulations and University policies designed to protect the rights and welfare of participants in research.

13. Will my study-related information be kept confidential?

Efforts will be made to keep your study-related information confidential. However, there may be circumstances where this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law.

Also, your records may be reviewed by the following groups (as applicable to the research):

- Office for Human Research Protections or other federal, state, or international regulatory agencies;
- U.S. Food and Drug Administration;
- The Ohio State University Institutional Review Board or Office of Responsible Research Practices;
- The sponsor supporting the study, their agents or study monitors; and
- Your insurance company (if charges are billed to insurance).
- The National Institutes of Health

If this study is related to your medical care, your study-related information may be placed in your permanent hospital, clinic, or physician's office records. Authorized Ohio State University staff not involved in the study may be aware that you are participating in a research study and have access to your information.

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

You may also be asked to sign a separate Health Insurance Portability and Accountability Act (HIPAA) research authorization form if the study involves the use of your protected health information.

A new Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also will not protect you against discrimination based on a previously diagnosed genetic disease or condition. GINA's provisions prohibiting discrimination by employers based on genetic information generally do not apply to employers with fewer than 15 employees.

The NIH issues Certificates of Confidentiality for all NIH-funded studies, including this study. This Certificate provides extra protection for you and your study information, documents, or samples (blood, tissue, etc.). The Certificates are issued so that we cannot be required to disclose any identifiable information collected about you as a part of this study in a lawsuit or legal proceeding. This is a layer of protection over and above the already existing protections in place for you and your information, documents, or samples.

However, these protections do not apply in some situations. For example, we may have to release your information if a law requires us to do so, if the NIH and ARIAD that is funding this study requests the information, or if the FDA tells us to release this information.

Please talk to your study team, or contact the Office of Responsible Research Practices at 614-688-8641, if you have questions.

Please visit the NIH website at https://humansubjects.nih.gov/coc/faqs to learn more.

14. HIPAA AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

I. What information may be used and given to others?

- Past and present medical records;
- Research records;
- Records about phone calls made as part of this research;
- Records about your study visits;
- Information that includes personal identifiers, such as your name, or a number associated with you as an individual;
- Information gathered for this research about:
  HIV / AIDS
  Physical exams

Laboratory, x-ray, and other test results
Diaries and questionnaires
The diagnosis and treatment of a mental health condition

- Records about any study drug you received;

II. Who may use and give out information about you?

Researchers and study staff.

III. Who might get this information?

- The sponsor of this research. "Sponsor" means any persons or companies that are:
  - working for or with the sponsor; or
  - owned by the sponsor.
- Authorized Ohio State University staff not involved in the study may be aware that you are participating in a research study and have access to your information;
- If this study is related to your medical care, your study-related information may be placed in your permanent hospital, clinic or physician's office record;
- Others: Takeda, the Drug Sponsor for this trial

IV. Your information <u>may</u> be given to:

- The U.S. Food and Drug Administration (FDA), Department of Health and Human Services (DHHS) agencies, and other federal and state entities;
- Governmental agencies in other countries;
- Governmental agencies to whom certain diseases (reportable diseases) must be reported; and
- The Ohio State University units involved in managing and approving the research study including the Office of Research and the Office of Responsible Research Practices.

V. Why will this information be used and/or given to others?

- To do the research;
- To study the results; and
- To make sure that the research was done right.

VI. When will my permission end?

There is no date at which your permission ends. Your information will be used indefinitely. This is because the information used and created during the study may be analyzed for many years, and it is not possible to know when this will be complete.

VII. May I withdraw or revoke (cancel) my permission?

Yes. Your authorization will be good for the time period indicated above unless you change your mind and revoke it in writing. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the researchers. If you withdraw your permission, you will not be able to stay in this study. When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

VIII. What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study and receive research-related treatment. However, if you are being treated as a patient here, you will still be able to receive care.

IX. Is my health information protected after it has been given to others?

There is a risk that your information will be given to others without your permission. Any information that is shared may no longer be protected by federal privacy rules.

X. May I review or copy my information?

Signing this authorization also means that you may not be able to see or copy your study-related information until the study is completed.

15. Who can answer my questions about the study?

For questions, concerns, or complaints about the study you may contact **Sameek Roychowdhury, MD, PhD at (614) 293-6196.**

For questions about your rights as a participant in this study or to discuss other study-related concerns or complaints with someone who is not part of the research team, you may contact **Ms. Sandra Meadows in the Office of Responsible Research Practices at 1-800-678-6251.**

For questions related to your privacy rights under HIPAA or related to this research authorization, please contact:

HIPAA Privacy Officer
Suite E2140, 600 Ackerman Road
Columbus, Ohio 43201
Telephone: 614-293-4477

If you are injured as a result of participating in this study or for questions about a study-related injury, you may contact **Sameek Roychowdhury, MD, PhD at (614) 293-6196.**

Signing the consent form

I have read (or someone has read to me) this form and I am aware that I am being asked to participate in a research study. I have had the opportunity to ask questions and have had them answered to my satisfaction. I voluntarily agree to participate in this study.

I am not giving up any legal rights by signing this form. I will be given a copy of this form**.**

Printed name of subject	**Signature of subject**
	AM/PM
	Date and time
Printed name of person authorized to consent for subject (when applicable)	**Signature of person authorized to consent for subject (when applicable)**
	AM/PM
Relationship to the subject	**Date and time**

Investigator/Research Staff

I have explained the research to the participant or his/her representative before requesting the signature(s) above. There are no blanks in this document. A copy of this form has been given to the participant or his/her representative.

Printed name of person obtaining consent	**Signature of person obtaining consent**
	AM/PM
	Date and time

Witness(es) - *May be left blank if not required by the IRB*

Printed name of witness	**Signature of witness**
	AM/PM
	Date and time
Printed name of witness	**Signature of witness**
	AM/PM
	Date and time