Official title: Pacritinib for Biochemical Relapse After Definitive Treatment for Prostate Cancer

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MCW IRB

Medical College of Wisconsin
INTRODUCTION TO THE INFORMED CONSENT

IIT-KILARI-J31001-BLAST: A Single-Arm, Open-Label, Phase 2 Study Evaluating PacritiniB for Patients with BiochemicaL RelApse after Definitive Treatment for ProStaTe Cancer

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Definitions

Biomarker – something found in the blood, other fluids, or tissues that can be used to measure the progress of disease or how a treatment is working

Purpose

This project is being done to test the effectiveness of a new drug called Pacritinib. Researchers would also like to study how Pacritinib slows down the time until cancer progression and assess its safety and tolerability.

Length

1. You will be in this research project for about 2 years.
- We would also like to follow you for every 6 months for 2 years to monitor how you are doing.

Procedures

All subjects in this study will be treated with Pacritinib. Pacritinib will be administered in 28-day cycles.

List of visits:

- Screening Visit(s)
  - Total Number: approx. 1-3
  - Total Time: approx. 6-12 hours
- Treatment Visits
  - Total Number: until your cancer progresses
  - Total Time: approx. 2-4 hours each
- End of Treatment Visit(s)
  - Total Number: approx. 1-2
  - Total Time: approx. 2-3 hours

Procedures that will occur at various visits:

Invasive Procedures

- Blood collection for routine laboratory tests and research tests
- Tumor assessments by CT/MRI/Bone scan

Non-invasive Procedures

- Physical exam and vital signs
- Heart monitoring by Electrocardiogram (ECG) and Echocardiogram (ECHO)
- Performance Status
- Quality of Life questionnaires

Risks

This is a brief list of the most commonly seen side effects. The ***full consent form*** after this introduction contains a more complete list of potential research risks.

Pacritinib risks:

- Gastrointestinal side effects such as diarrhea (loose, watery stools), nausea, vomiting
- General side effects such as fatigue (feeling very tired), fever, and swelling of limbs (peripheral edema)
- Decreased amounts of red blood cells (anemia), platelet cells (thrombocytopenia), and white blood cells (neutropenia)
- Abnormal blood cell counts (leukopenia) and fever associated with low white blood cell count (febrile neutropenia)
- Bleeding in the throat (pharyngeal hemorrhage), digestive tract (esophageal varices hemorrhage), brain (cerebral hemorrhage and subdural hematoma), stroke (cerebrovascular accident), and nosebleeds (epistaxis)
- Abnormal heart rhythm (prolonged QT, bradycardia, cardiac fibrillation, sinus tachycardia, and atrioventricular [A-V] block)
- Cardiac and vascular conditions (angina pectoris, myocardial ischemia, hypertensive crisis), cardiac inflammation (pericarditis), heart attack (myocardial infarction), and cardiac failure (including congestive heart failure)

Benefits

We don't know if this project will help you. Your condition may get better but it could stay the same or even get worse.

My Other Options

You do not have to join this project. Your other options may include:

1. Joining a different project
2. Routine care for this condition
3. Getting no treatment for this condition

If you have more questions about this project at any time, you can call Deepak Kilari, MD at 414-805-6700

If you have questions about your rights as a participant, want to report any problems or complaints, or offer input, you can call the MCW/Froedtert Hospital Research Subject Advocate at 414-955-8844.

CONSENT TO PARTICIPATE IN RESEARCH

A1. INTRODUCTION – WHY ARE WE ASKING YOU TO PARTICIPATE?

You are being invited to participate in this research because you have prostate adenocarcinoma that has recurred (come back again) after a radical prostatectomy surgery or radiation therapy.

A total of about 46 people are expected to participate in this research at the Medical College of Wisconsin/Froedtert Hospital.

The Director of the project is Deepak Kilari, MD in the Department of Medicine. A research team works with Dr. Kilari. You can ask who these people are.

CTI BioPharma, a pharmaceutical company that produces the study drug Pacritinib, is funding this study. The study is also being funding by Cancer Center funds.

A2. DO I HAVE TO PARTICIPATE?

You can decide whether to take part in this research or not. You are free to say yes or no. If you do not agree to join, or if you leave, you will not be penalized or lose any benefits that you had before starting the research project. Even if you join this project, you do not have to stay in it. You may stop at any time. Take as much time as you need to make your choice.

A research project is different from routine medical care in three ways: 1) there are extra risks that we will tell you about in this form; 2) you may have some extra medical tests and visits; 3) the research procedures, tests and visits follow a set plan that must be kept.

A3. WHY IS THIS PROJECT BEING DONE?

The most common standard of care treatment for recurrent prostate cancer, Androgen Deprivation Therapy (ADT), tries to slow down the growth of cancer cells by reducing the level of male hormones. However, there are many common side effects associated with these drugs due to resulting lower levels of testosterone in the body. Patients treated with ADT report lower quality of life because of the side effects. Current standard of care treatment is usually continued for life, so it is a priority to develop new prostate cancer therapy options with fewer side effects.

The purpose of this study is to test the effectiveness of a new drug called Pacritinib. Researchers would also like to study how Pacritinib slows down the time until cancer progression. They would also like to assess the safety and toxicity of Pacritinib and see how it compares with standard of care treatments. Pacritinib is investigational in this study, meaning it has not been approved by the FDA for the treatment of prostate cancer. In addition, although Pacritinib has been studied to treat other cancers, it has not previously been tested in other clinical trials as a treatment for prostate cancer.

We don’t know if this study will help you. Your condition may get better, but it could stay the same or even get worse. We hope the information from this study will help us develop a better treatment for prostate cancer in the future.

B1. WHAT WILL HAPPEN IF I PARTICIPATE?

STUDY DRUG

If you participate in the study, Pacritinib will be taken orally (by mouth) as a capsule. The capsules should not be opened or crushed. If the capsule if crushed or damaged, you should not touch the powder inside the capsule as it may irritate the skin or mucous membranes (e.g. inside of the nose). You should store Pacritinib capsules at room temperature.

Pacritinib will be administered in 28-day cycles. You will take two 100 mg Pacritinib capsules (200 mg Pacritinib in each dose) twice daily, for a total of 400 mg each day. The two doses should be taken about 12 hours apart. You will be asked to complete a Subject Diary to record when you take each dose of Pacritinib and any side effects you may experience. You will return to the clinic at the beginning of each cycle to receive an additional supply of Pacritinib. You should bring any remaining Pacritinib capsules and the Subject Diary with you to all study visits.

STUDY GROUP

All subjects in this study will be treated with Pacritinib. The study is open label, meaning you, your study doctor, and other members of the study team will know your treatment.

STUDY VISITS

Screening
If you agree to participate in the study, you will sign this consent form before screening assessments are performed to see if you are eligible. Your study doctor or a member of the study team will let you know if you are eligible to participate in the study. If you are unable to participate in the study, the study doctor will discuss other treatment options with you.

Treatment
If you are eligible to participate, you will begin Pacritinib treatment as described above. You will return to the clinic on Day 1 and Day 15 during Cycle 1, on Day 1 during Cycles 2-5, and then every other cycle from Cycle 6 and beyond. Assessments to track your disease status and to monitor you for side effects will occur during the treatment visits. You will continue Pacritinib treatment about 2 years. If your study doctor thinks that you may benefit from continued Pacritinib treatment beyond 2 years, the treatment period may be extended.

Follow-up
After you stop Pacritinib treatment, you will return to the clinic 30 days after your last dose for an End of Treatment visit to monitor for any side effects of the study drug. You will then return to the clinic every 6 months for 2 years to monitor how you are doing.

STUDY ASSESSMENTS

Screening
You will need to have all or some of the following exams, tests, or procedures to find out if you can be in the study. Some of them are routine and may be done even if you do not join the study. If some of the tests were completed recently, they may not have to be repeated.

- Informed consent: Prior to any study-related procedures being performed, you will be required to voluntarily sign and date this consent form.
- Medical history: You will be asked about your health status, including previous treatments for your cancer, and demographic information
- Medications: You will be asked about your current medications, including over-the-counter medications, vitamins, and herbal supplements
- Physical examination: You will receive a complete physical examination
- Vital signs: Your blood pressure, heart rate, respiratory rate, temperature, and weight will be checked
- Performance status: An assessment of your overall health and ability to perform daily tasks
- Electrocardiogram (ECG) and Echocardiogram (ECHO): ECG and ECHO will be performed to check the activity of your heart
- Blood tests: Blood samples will be collected for
    - PSA and testosterone levels
    - Blood cell counts, blood chemistry, clotting ability, and organ function
- CT/MRI/PET/Bone scan: You will have a tumor assessment by CT, MRI, PET, and/or bone scan to assess the size and location of cancer
- FACT-P Quality of Life and Comprehensive Geriatric Assessment questionnaires: Questions about daily activities and mental, physical, and emotional symptoms, etc.

Treatment
You will begin Pacritinib treatment if the results of screening assessments show that you are eligible.

Cycle 1 Day 1
The following assessments will be performed:

- Adverse events: You will be asked about if you experienced any changes in your health
- Medications: You will be asked about any changes in your current medications, including over-the-counter medications, vitamins, and herbal supplements
- Physical examination: You will receive a complete physical examination
- Vital signs: Your blood pressure, heart rate, respiratory rate, temperature, and weight will be checked
- Performance status: An assessment of your overall health and ability to perform daily tasks
- Electrocardiogram (ECG): ECG will be performed to check the activity of your heart
- Blood tests: Blood samples will be collected for

- PSA level
- Blood cell counts, blood chemistry, and organ function

Cycle 1 Day 15
The following assessments will be performed:

- Adverse events: You will be asked about if you experienced any changes in your health
- Medications: You will be asked about any changes in your current medications, including over-the-counter medications, vitamins, and herbal supplements
- Vital signs: Your blood pressure, heart rate, respiratory rate, temperature, and weight will be checked
- Performance status: An assessment of your overall health and ability to perform daily tasks
- Blood tests: Blood samples will be collected for
  - Blood cell counts, blood chemistry, and organ function

Cycle 2 Day 1
The following assessments will be performed:

- Adverse events: You will be asked about if you experienced any changes in your health
- Medications: You will be asked about any changes in your current medications, including over-the-counter medications, vitamins, and herbal supplements
- Physical examination: You will receive a complete physical examination
- Vital signs: Your blood pressure, heart rate, respiratory rate, temperature, and weight will be checked
- Performance status: An assessment of your overall health and ability to perform daily tasks
- Electrocardiogram (ECG) and Echocardiogram (ECHO): ECG and ECHO will be performed to check the activity of your heart
- Blood tests: Blood samples will be collected for
  - PSA level
  - Blood cell counts, blood chemistry, and organ function

Cycle 3 Day 1
The following assessments will be performed:

- Adverse events: You will be asked about if you experienced any changes in your health
- Medications: You will be asked about any changes in your current medications, including over-the-counter medications, vitamins, and herbal supplements
- Physical examination: You will receive a complete physical examination

- Vital signs: Your blood pressure, heart rate, respiratory rate, temperature, and weight will be checked
- Performance status: An assessment of your overall health and ability to perform daily tasks
- Blood tests: Blood samples will be collected for
    - PSA level
    - Blood cell counts

Cycle 4 Day 1
The following assessments will be performed:

- Adverse events: You will be asked about if you experienced any changes in your health
- Medications: You will be asked about any changes in your current medications, including over-the-counter medications, vitamins, and herbal supplements
- Physical examination: You will receive a complete physical examination
- Vital signs: Your blood pressure, heart rate, respiratory rate, temperature, and weight will be checked
- Performance status: An assessment of your overall health and ability to perform daily tasks
- Blood tests: Blood samples will be collected for
    - PSA and testosterone levels
    - Blood cell counts
- CT/MRI/PET/Bone scan: You will have a tumor assessment by CT, MRI, PET, and/or bone scan to assess the size and location of cancer
- FACT-P Quality of Life and Comprehensive Geriatric Assessment questionnaires: Questions about daily activities and mental, physical, and emotional symptoms, etc.

Cycle 5 Day 1
The following assessments will be performed:

- Adverse events: You will be asked about if you experienced any changes in your health
- Medications: You will be asked about any changes in your current medications, including over-the-counter medications, vitamins, and herbal supplements
- Physical examination: You will receive a complete physical examination
- Vital signs: Your blood pressure, heart rate, respiratory rate, temperature, and weight will be checked
- Performance status: An assessment of your overall health and ability to perform daily tasks

- Electrocardiogram (ECG) and Echocardiogram (ECHO): ECG and ECHO will be performed to check the activity of your heart
- Blood tests: Blood samples will be collected for
    - PSA level
    - Blood cell counts

Cycle 6 and beyond
The following assessments will be performed:

- Adverse events: You will be asked about if you experienced any changes in your health
- Medications: You will be asked about any changes in your current medications, including over-the-counter medications, vitamins, and herbal supplements
- Physical examination: You will receive a complete physical examination
- Vital signs: Your blood pressure, heart rate, respiratory rate, temperature, and weight will be checked
- Performance status: An assessment of your overall health and ability to perform daily tasks
- Electrocardiogram (ECG) and Echocardiogram (ECHO): ECG and ECHO will be performed to check the activity of your heart. ECG will be performed every 4 months. ECHO will be performed every 6 months.
- Blood tests: Blood samples will be collected for
    - PSA level
    - Blood cell counts and blood chemistry

At progression
The following assessments will be performed:

- Adverse events: You will be asked about if you experienced any changes in your health
- Medications: You will be asked about any changes in your current medications, including over-the-counter medications, vitamins, and herbal supplements
- Physical examination: You will receive a complete physical examination
- Vital signs: Your blood pressure, heart rate, respiratory rate, temperature, and weight will be checked
- Performance status: An assessment of your overall health and ability to perform daily tasks
- Blood tests: Blood samples will be collected for
    - PSA level
    - Blood cell counts, blood chemistry, and organ function

- CT/MRI/PET/Bone scan: You will have a tumor assessment by CT, MRI, PET, and/or bone scan to assess the size and location of cancer
- FACT-P Quality of Life questionnaire: Questions about daily activities and mental, physical, and emotional symptoms, etc.

Follow-up
End of Treatment Visit
The following assessments will be performed 30 days after you stop Pacritinib treatment:

- Adverse events: You will be asked about if you experienced any changes in your health
- Medications: You will be asked about any changes in your current medications, including over-the-counter medications, vitamins, and herbal supplements
- Physical examination: You will receive a complete physical examination
- Vital signs: Your blood pressure, heart rate, respiratory rate, temperature, and weight will be checked
- Performance status: An assessment of your overall health and ability to perform daily tasks
- Blood tests: Blood samples will be collected for
    - PSA level
    - Blood cell counts, blood chemistry, and organ function

Follow-up Visits
You will return to the clinic every 6 months for 2 years to monitor your health. The following assessments will be performed at each Follow-up Visit:

- Physical examination: You will receive a complete physical examination
- Performance status: An assessment of your overall health and ability to perform daily tasks
- Blood tests: Blood samples will be collected for
    - PSA level

SAMPLES FOR RESEARCH

You will be asked to provide the following samples to be used for biomarker research:

Tumor tissue
- Archival tissue from previous biopsies, if sufficient tissue is available

Blood samples
- Cycle 1 Day 1
- Cycle 2 Day 1
- Cycle 4 Day 1
- At time of progression

The samples will be used to analyze different biomarkers. A biomarker is something found in the blood, other fluids, or tissues that can be used to measure the progress of disease or how a treatment is working. This future research will be related to this current study. Allowing your tumor tissue and blood samples to be used for biomarker research is optional. You may still participate in the study even if you do not allow your samples to be used for biomarker research.

I agree that my tumor tissue and blood samples can be used for biomarker research **Yes** ☐ **No** ☐

GENETIC TESTING

In this study, we will do genetic testing on your biospecimens. Whole genome sequencing may be included as part of the genetic testing for this research. This will be collected at the visits listed in the "SAMPLES FOR RESEARCH" heading above. Genetic testing will be done because researchers would like to better understand how genes affect health and response to treatment.

This genetic testing is for research only. The purpose is not to discover information that could be used to change your medical care, make or change your diagnosis, or advise you on your risk of diseases.

The biospecimens collected for this part of the study will be coded, which means they will be labeled with numbers and/or letters instead of information that could identify you. Only the research team will be able to link the code to you. The samples will also be labeled with date of collection, which could potentially be used to identify you. The research team will make every effort to protect the information and keep it confidential, but it is possible that an unauthorized person might see it. Depending on the kind of information being collected, it might be used in a way that could embarrass you.

It is against federal law (Genetic Information Nondiscrimination Act, or GINA) for health insurance companies to deny health insurance, or large employers to deny jobs, based on your genetic information. But the same law does not protect your ability to get disability, life, or long-term care insurance. If you have questions, you can talk to the research doctor about whether this could apply to you.

You will not be given your genetic test results.

B2. HOW LONG WILL I BE IN THE PROJECT?

You will continue Pacritinib treatment for about 2 years. If your study doctor thinks that you may benefit from continued Pacritinib treatment beyond 2 years, the treatment period may be extended.

After you stop Pacritinib treatment, you will return to the clinic 30 days after your last dose for an End of Treatment visit to monitor for any side effects of the study drug. You will then return to the clinic every 6 months for 2 years to monitor how you are doing.

B3. CAN I STOP BEING IN THE PROJECT?

You are free to withdraw from the project at any time. If you leave, your regular medical care will not change. If you are thinking about leaving, please tell the research doctor.

The research doctor can tell you about the effects of stopping, and you and the research doctor can talk about what follow-up care would help you the most.

You might be asked to come back for follow-up visit(s) to check your health.

You might be asked to return your research drug containers.

The research doctor may take you out of this project at any time. This would happen if:

- They think it is in your best interest.
- You do not follow the project rules.
- The whole project is stopped.

If this happens, the research doctor will tell you.

B4. ARE THERE ANY SPECIAL INSTRUCTIONS WHILE I AM IN THE PROJECT?

You should tell the study doctor of any changes in your current medications, including over-the-counter medications, vitamins, and herbal supplements. Some medications are not allowed during the study. Your study doctor will advise about which medications these are.

You should bring remaining study drug and the Subject Diary to all treatment visits.

C1. WHAT HEALTH RISKS OR PROBLEMS CAN I EXPECT FROM THE PROJECT?

There are risks to taking part in any research project. There is a risk that you may get a drug that does not help your condition or may make it worse. There also may be problems (side effects) we do not know about yet, from the drug itself, or how it combines with other drugs you are taking. If we learn about new important side effects, we will tell you.

We watch everyone in the project for problems (side effects). **You need to tell the research doctor or a member of the research team immediately if you experience any problems, side effects, or changes in your health.** In an emergency, call 911.

C2. RISKS OF PACRITINIB

The research drug itself may cause problems (side effects). Side effects may be mild or very serious. Some can last a long time or never go away.

Pacritinib has been given to approximately 1128 patients in 16 completed studies. Based on the adverse effects reported from the completed studies, the main identified risks for Pacritinib included gastrointestinal events, bleeding, and cardiac events.

Life-threatening and sometimes fatal cardiac events have been observed in participants treated with Pacritinib, including heart failure and arrhythmias, some of which may have been associated with sudden death.

Serious bleeding events, specifically bleeding of the brain (intracranial hemorrhage, subdural hematoma, and cerebral hemorrhage), have been observed in association with Pacritinib treatment occasionally with life-threatening or fatal outcomes.

Very common side effects occurring in at least 10% of participants who received Pacritinib include:

- Gastrointestinal side effects such as diarrhea (loose, watery stools), nausea, vomiting
- General side effects such as fatigue (feeling very tired), fever, and swelling of limbs (peripheral edema)
- Decreased amounts of red blood cells (anemia), platelet cells (thrombocytopenia), and white blood cells (neutropenia)

Common side effects occurring in 1% to 10% of those who received Pacritinib include:

- Abnormal blood cell counts (leukopenia) and fever associated with low white blood cell count (febrile neutropenia)
- Bleeding in the throat (pharyngeal hemorrhage), digestive tract (esophageal varices hemorrhage), brain (cerebral hemorrhage and subdural hematoma), stroke (cerebrovascular accident), and nosebleeds (epistaxis)
- Abnormal heart rhythm (prolonged QT, bradycardia, cardiac fibrillation, sinus tachycardia, and atrioventricular [A-V] block)
- Cardiac and vascular conditions (angina pectoris, myocardial ischemia, hypertensive crisis), cardiac inflammation (pericarditis), heart attack (myocardial infarction), and cardiac failure (including congestive heart failure)
- Gastrointestinal effects including abdominal pain, fluid in abdomen, poor appetite, dehydration, and weight changes
- Cancers of skin
- Changes in laboratory results such as elevated bilirubin in the blood, increased liver enzymes (indicating liver damage), high levels of uric acid in the blood (hyperuricemia and gout), abnormal blood glucose (including diabetes mellitus), and electrolyte changes
- General effects such as shortness of breath, weakness (including muscles), numbness and pain of limbs, headache, low blood pressure, dizziness and vertigo, syncope, and fall
- Kidney and bladder disorders including kidney failure and kidney stones
- Reproductive tract disorders such as inflammation of testes (orchitis and epididymitis)
- Skin disorders (rash and itching)
- Infections including abscess, gastroenteritis, pneumonia, bronchitis, and urinary tract infection

Uncommon side effects occurring in less than 1% of participants who received Pacritinib which could be potentially life-threatening include:

- Pulmonary conditions (pulmonary arterial hypertension, pulmonary embolism, pulmonary infarction, and interstitial lung disease) and other respiratory effects (fluid in lungs, acute

respiratory distress syndrome, and respiratory failure)

- Severe infections (bacterial/viral/fungal, with possible sepsis, shock, and organ failure)
- Digestive tract disorders (diverticular perforation - diverticula are small, bulging pouches that can form in the lining of your digestive system; most often found in the lower part of the large intestine) and hepatic disorders (portal hypertension - an increase in the pressure within the portal vein (the vein that carries blood from the digestive organs to the liver). The increase in pressure is caused by a blockage in the blood flow through the liver.
- Transformation into Acute Myeloid Leukemia (AML)

Ask the study doctor or study staff if you have questions about the signs or symptoms of any side effects you read about in this consent form.

Could I have an allergic reaction?
Sometimes people have allergic reactions to drugs. If you have a very bad allergic reaction, you could die. Some things that happen during an allergic reaction that could be a sign or symptom of a life-threatening allergic reaction (anaphylaxis) are:

- A rash or hives
- Having a hard time breathing
- Wheezing when you breath
- A sudden drop in blood pressure (making you feel dizzy or lightheaded)
- Swelling around the mouth, throat, or eyes
- A fast pulse
- Sweating

You should get immediate medical help and contact the study doctor or study staff if you have any of these or any other side effects during the study.

C3. OTHER RISKS OF THIS RESEARCH PROJECT

Other procedures that are part of the research also involve some risks:

Electrocardiogram (ECG)
An ECG procedure requires you to lie still for a few minutes while electrodes are attached to your chest, wrists, and ankles to record the activity of your heart. The ECG leads placed on your skin may cause slight discomfort during their placement and removal.

Echocardiogram (ECHO)
During the echocardiogram, electrodes will be placed onto your chest to allow for an ECG to be performed. Then a transducer (a device that looks like a computer mouse) will be applied. You may feel slight pressure on your chest from the transducer. In addition, you may be asked to breathe in a certain way or to rest on your side during the test.

Blood collection
Blood collection may cause some discomfort, bleeding, or bruising at the puncture site. A small blood crust or swelling may occur at this site. In rare cases, fainting or local infection may occur. If you feel discomfort during blood collection, please report this to the study doctor or staff at the time.

Computed Tomography (CT Scan)
CT scans use x-rays to create an image. If frequent CT scans are performed, the cumulative amount of radiation involved could be concerning. The mean effective dose from a diagnostic abdomen and pelvis CT procedure is around 10 mSv, which is equivalent to natural background radiation for around 3 years. People who have a small but increased radiation exposure may have the risk of cancer development in later life. However, there is considerable uncertainty regarding the risk estimates for low levels of radiation exposure from the CT scans you will undergo.

Magnetic Resonance Imaging (MRI Scan)
MRI, which uses a large magnet instead of x-rays to take pictures of your body, you may feel mild vibrations throughout your body. The machine will produce a loud knocking noise. This is normal. You will be given earplugs to protect your ears. Some people, especially those who tend to feel uncomfortable in small or closed spaces, may feel “closed in” and become anxious while in the scanner. The scanner has an intercom, which will allow you to speak to the staff during the procedure. If you feel ill or anxious during scanning, tell the MRI staff and the scanning will be stopped if you wish.

The MRI will require a catheter to be inserted into one of your veins in order to inject the MRI contrast agent. This may cause skin irritation, bleeding, and/or infection. You may have an allergic reaction to the contrast agent.

The magnetic field used in MRI scanning may harm people who have metal in their bodies (pacemakers, neurostimulators, certain clips, or staples from surgery). It may cause problems with devices, such as pacemakers. If you have metal in your body or a pacemaker, you should not have an MRI. Your study doctor will discuss with you whether you should have a MRI scan with a contrast agent based on your health status.

Bone scan
During a bone scan, a radioactive substance called a tracer is injected into a vein. The tracer travels through your bloodstream and into your bones. The tracers in the radioactive dye used in a bone scan produce very little radiation exposure. Then a special camera takes pictures of the tracer in your bones. Areas that absorb little or no amount of tracer appear as dark or ‘cold’ spots, while areas that concentrate the tracer appear as ‘hot’ spots.

PET-CT
Positron emission tomography (PET) is a type of imaging test that uses a small amount of radioactive material injected into your vein to see how cells or tissues are functioning. Before the scan, you will have to follow preparation instructions including not eating for 6 hours before the test. After the PET agent is injected, you will wait 45-60 minutes before being scanned. The scan will take several minutes, and you must lie still during that time.

Risks of Questions on Your Well-Being
The answers that you give are confidential, but there is always a risk that your answers will be read by people who should not read your personal information. You may also feel uncomfortable answering some of the questions.

Privacy and Confidentiality
Another risk may be loss of confidentiality. Every effort will be made to keep your research records confidential but we cannot guarantee it. Depending on the kind of information being collected, if your research information were accidentally seen, it might be used in a way that could embarrass you or affect your ability to get insurance. If you have questions, you can talk to the project director about whether this could apply to you.

C4. REPRODUCTIVE RISKS

Risks to a subject's partner(s)
If you and your partner(s) are able to become pregnant, one or both of you must use some form of effective birth control, because it is unknown if the study drug could affect a baby. You must tell the research doctor right away if you think your partner is pregnant.

You may not donate sperm during your participation in the project or for 90 days after stopping the study drug.

Birth control methods for all subjects
Check with the research doctor about the birth control methods needed for this project and how long to use them. Some methods might not be good enough for this project. If you are having sex that could lead to pregnancy, you should use two forms of highly effective birth control while you are in this project.

This may include:

- Not having vaginal sex (abstinence)
- Taking birth control pills orally
- Having birth control shots or patches such as Depo-Provera
- Surgical sterilization (hysterectomy/tubal ligation or vasectomy)
- Limiting sexual activity to a partner who has undergone surgical sterilization
- Use of an intrauterine device (IUD)
- Use of diaphragm with contraceptive jelly
- Use of condoms with contraceptive foam
- Use of diaphragm with condoms ("double barrier")

You should continue using birth control for 90 days after stopping the study drug.

C5. ARE THERE ANY BENEFITS TO TAKING PART IN THE PROJECT?

We don't know if this study will help you. Your condition may get better but it could stay the same or even get worse. We hope the information from this study will help us develop better treatments for prostate cancer.

D1. ARE THERE ANY COSTS TO BEING IN THE PROJECT?

Most of the medical care that you will receive in this project is considered routine care for your condition and would be recommended whether or not you join the project. Costs for routine care will be billed to you or your insurance carrier. For routine clinical care, you will be responsible for paying any copayment, coinsurance, or deductible that is required by your insurance carrier.

Activities / costs that are part of the project will not be billed to you or your insurance company. These are:

- Study drug (Pacritinib)
- Heartbeat tests (ECG, ECHO/TTE)
- Coagulation tests (PT/PTT/HbA1C)
- Cholesterol
- Collection, processing, and analysis of research specimens (tissue, blood)
- Any screening procedure if repeated

Some insurers will not pay for drugs, tests or hospitalization that are part of research, so check with your insurer before you join this project. If you have questions regarding costs, please contact Dr. Kilari.

If you participate in this research, the costs of any necessary emergency medical treatment in the event of a research-related injury will be billed to you or your health insurance.

D2. WILL I BE PAID FOR PARTICIPATING IN THE PROJECT?

There is no payment for being in this project.

Sponsor, other researchers, or research companies may patent or sell products, discoveries and data or information that result from this research. Neither Sponsor nor Dr. Kilari will pay you if this happens. You will not receive any payment or commercial rights for products, data, discoveries, or materials gained or produced from your health information/biospecimens.

D3. WHAT OTHER HEALTHCARE CHOICES DO I HAVE?

You do not have to join this project. You are free to say yes or no. If you do not join this project, your research doctor can discuss other healthcare choices with you.

Your other choices may include:

- Routine care for this condition or symptoms.
- Joining a different research project
- The procedure or drug offered to you may also be available without being in any research project.

The research doctor can explain both the possible benefits and the risks of other options that are available to you.

D4. WILL I BE GIVEN NEW INFORMATION ABOUT THE PROJECT?

If we learn any important new information about the drug that might change your mind about being in the project, we will tell you about it right away. You can then decide if you want to stay in the project.

When research biospecimens are collected and analyzed, there is the chance of finding something clinically relevant. There may be benefits to learning such results (such as early detection and treatment of a medical condition), but there are risks as well (such as feeling worried about a finding for which no treatment is required or appropriate).

The results from the biospecimens we collect in this research study are not the same quality as what you would receive as part of your health care, so you will not be informed of any clinically relevant research findings. The results of your research biospecimens will not be placed in your medical record.

D5. WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THE PROJECT?

Emergency medical treatment for injuries directly related to your participation in this research project will be provided to you. You or your health insurance will be billed for the costs of this emergency treatment. MCW will decide on a case by case basis if they will reimburse you or your insurer for emergency treatment costs. If your research-related injury requires medical care beyond this emergency treatment, you or your insurer will be responsible for the costs of this follow-up care.

At this time, there is no plan for any additional financial payments.

If you believe that you have been injured because of your participation in this project, contact the research doctors right away. Contact information: Deepak Kilari, 414-805-6700

Nothing in this consent form affects any legal rights you may have nor does it release the investigator, the sponsor, the institution, or its agents from liability for negligence.

D6. WHO CAN ANSWER MY QUESTIONS ABOUT THE PROJECT?

- If you have more questions about this project at any time, you can call Deepak Kilari, MD at 414-805-6700.
- If you have questions about your rights as a research participant, want to report any problems or complaints, or offer input, you can call the MCW/Froedtert Hospital Research Subject Advocate at 414-955-8844.

E. PERMISSION TO COLLECT, USE AND SHARE HEALTH INFORMATION

E1. What health information will be collected and used for this project?

To be in this research project, the research team needs your permission to access, collect and use some of your health information. If you say no, you cannot be in the project. This information may come from questions we ask, forms we ask you to fill out, or your medical record, as described below. We will only collect and use information needed for the project.

The protected health information (PHI) originates from services you will or have received at one or more of the following locations: the Medical College of Wisconsin (MCW); Versiti, Inc.; Children's Hospital of Wisconsin (CHW); any Froedtert Health Affiliate- Froedtert Hospital (FH), Inc.; Froedtert Menomonee Falls Hospital; Froedtert West Bend Hospital; Froedtert & The Medical College of Wisconsin Community Physicians Clinics, Inc. (FMCWCP); the West Bend Surgery Center, LLC; and the Froedtert Surgery Center, LLC.

The health information to be collected and used for this project is:

- Past and present medical records to document relevant preexisting conditions
- Records about your study visits and results of tests done during the study
- Records about phone calls made as part of this research
- Research records

E2. Who will see the health information collected for this project?

The only MCW/Froedtert Hospital. employees allowed to handle your health information are those on the research team, those on the Institutional Review Board (IRB) and those who check on the research activities to make sure the hospital's rules are followed.

If the costs of any necessary emergency medical treatment in the event of a research-related injury are billed to your health insurance, your health information may need to be disclosed to the insurer for billing purposes.

The research team may share your information with people who don't work at MCW/Froedtert Hospital because they planned, pay for, or work with us on this project. The federal Privacy Rule may no longer protect your health information once it leaves MCW/Froedtert Hospital. For this project, we plan to share information with those doctors, researchers or government representatives working with us on this project at the institutions or companies listed here:

- The pharmaceutical company providing study drug, CTI Biopharma, and its research partners;
- Government agencies in the U.S., such as the Food and Drug Administration (FDA), National Cancer Institute (NCI), and National Institutes of Health (NIH);
- Other federal and state agencies, such as the Office of Human Research Protections, (OHRP);
- Others required by law
- Florence Healthcare, Inc.

Because this project involves the use of drugs and/or devices, the FDA also has the right to inspect all project records.

We may record your research information, including results of tests and procedures done for research, in your Froedtert Hospital and/or Medical College of Wisconsin medical record. As a result, this research information may be seen by people allowed to see your medical records for healthcare operations or treatment, by those you allow to see your medical records by giving written permission, and by others when required by law.

We will not use your personal health information for a different project without your permission or the permission of a hospital research review board (IRB). Once all personal identification is removed from your health information and/or biospecimens, the information and/or biospecimens may be used for future research or distributed to another investigator for future research without additional informed consent from you or your legally authorized representative. The information might also be used or released for other purposes without asking you. Results of the project may be presented in public talks or written articles, but no information will be presented that identifies you.

E3. What are the risks of sharing this health information?

One risk of taking part in a research project is that more people will handle your personal health information collected for this project. The research team will make every effort to protect the information and keep it confidential, but it is possible that an unauthorized person might see it. If you have questions, you can talk to the research doctor about whether this could apply to you.

E4. How long will you keep the health information for this project?

If you sign this form, we plan to keep your information without any end-date in case we need to check it again for this project.

E5. Can I cancel my permission to share this health information?

If you change your mind later and do not want us to collect or share your health information, you need to send a letter to Deepak Kilari, MD at

Department of Medicine
Medical College of Wisconsin
8701 Watertown Plank Road
Milwaukee WI 53226

The letter must say that you have changed your mind and do not want the researcher to collect and share your health information. At that time, we will decide that you cannot continue to be part of the project. We may still use the information we have already collected.

E6. Access to records

You may not be able to see, or copy, your project-related health information until after the project has been completed; otherwise, it could affect the study.

F1. FOR MORE INFORMATION ABOUT THE PROJECT

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 look up this project by referring to the ClinicalTrials.gov number (NCT04635059) or by asking the research team for a printed copy.

CONSENT TO PARTICIPATE

By signing my name below, I confirm the following:

- I have read (or had read to me) this entire consent document. All of my questions have been answered to my satisfaction.
- The project's purpose, procedures, risks and possible benefits have been explained to me.
- I agree to let the research team use and share the health information and other information gathered for this project.
- I voluntarily agree to participate in this research project. I agree to follow the procedures as directed. I have been told that I can stop at any time.

IMPORTANT: You will receive a signed and dated copy of this consent form. Please keep it where you can find it easily. It will help you remember what we discussed today.

Subject's Name *please print*	**Subject's Signature**	**Date**
Name of Witness, if applicable *please print*	**Signature of Witness**	**Date**
Rationale for Use of Witness ☐ Subject has limited/no literacy ☐ Subject has limited English proficiency ☐ Subject has limited/no vision	☐ Sponsor requirement ☐ Other _____	
*** Name of person discussing/ obtaining consent** *please print*	**Signature of person discussing/obtaining consent**	**Date**

** A member of the research team trained and authorized by the Principal Investigator to act on her/his behalf in obtaining informed consent according to the protocol. The Principal Investigator is responsible and accountable for the research project.*