IRB APPROVED
Sep 25, 2024

Informed Consent/Authorization for Participation in Research

TITLE: Brigatinib plus chemotherapy or local consolidation therapy in ALK positive advanced non-small cell lung cancer (BrightStar-2)

PROTOCOL NO.: 2024-0130
WCG IRB Protocol #20243161

SPONSOR: MD Anderson Cancer Center

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STUDY-RELATED PHONE NUMBER(S): 713-792-2121 (24 hours)

_____ _____
Participant's Name Medical Record Number

Your participation in this study is voluntary. You may decide not to participate or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits to which you are otherwise entitled.

If you have questions, concerns, or complaints, or think this research has hurt you, talk to the research team at the phone number(s) listed in this document.

Key Information

The following is a short summary of this study to help you decide whether or not to be a part of this study. More detailed information is listed later on in this form.

Why am I being invited to take part in a research study?

You are invited to take part in a research study because you have an advanced form of non-small cell lung cancer (NSCLC) that has a mutation (a type of genetic change) in the ALK gene.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.

- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?

The goal of this clinical research study is to learn if the combination of brigatinib and either local consolidation therapy (such as radiotherapy or surgery) or chemotherapy (pemetrexed and carboplatin) can help to control the disease compared with brigatinib alone. The safety of these combinations will also be studied.

This is an investigational study. The combination of brigatinib and either local consolidation therapy or chemotherapy (pemetrexed and carboplatin) is not FDA approved or commercially available. They are currently being used for research purposes only.

Brigatinib is FDA approved and commercially available for the treatment of metastatic (has spread to other parts of the body) ALK-positive NSCLC. Pemetrexed and carboplatin are FDA approved and commercially available for the treatment of non-squamous NSCLC.

The study doctor can explain how the study drugs are designed to work.

All participants will take brigatinib for 12 weeks. You will then be randomly assigned (the roll of the dice) to one of three groups:

1. Brigatinib only

2. Brigatinib with carboplatin and pemetrexed. Carboplatin and pemetrexed will be given intravenously every 3 weeks for 4 cycles. If you receive pemetrexed you will also receive dexamethasone, B12 injections and daily folic acid per your institutions guidelines.

3. Brigatinib plus local consolidation therapy (LCT).

The choice of the type of local consolidation therapy {(LCT)-i.e. surgery vs. stereotactic body radiation therapy (SBRT)} will be determined by a multidisciplinary team composed of thoracic radiation oncology, thoracic medical oncology, and thoracic surgical oncology. Note, however, that the final decision regarding the modality of LCT will be made at the treating physician’s discretion, after a consensus by the multidisciplinary team. Your physician will thoroughly review the local consolidation therapy with you.

How long will the research last and what will I need to do?

You may receive the study drug(s) for as long as the doctor thinks it is in your best interest and your cancer does not get worse.

You will be asked to receive the study drug(s) and return to the clinic for several visits, at which procedures will be performed for routine and research tests.

More detailed information about the study procedures can be found under ***"What happens if I agree to be in this research?"***

Is there any way being in this study could be bad for me?

Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects, potential expenses, and time commitment.

You may experience discomforts and risks associated with the administration of brigatinib study treatment and the study procedures. These potential discomforts and risks are based on information gained from studies of brigatinib administration in animals and early studies in humans. The predicted discomforts and risks vary from person to person. Your study doctor will discuss with you the possible discomforts and risks involved with the use of brigatinib.

More detailed information about the risks of this study can be found under ***"Is there any way being in this study could be bad for me? (Detailed Risks)"***

Will being in this study help me in any way?

It cannot be promised that there will be any benefits to you or others from your taking part in this research. However, the study drugs and procedures may help to control the disease. Future patients may benefit from what is learned.

What happens if I do not want to be in this research?

Participation in research is completely voluntary. You can decide to participate, not participate, or discontinue participation at any time without penalty or loss of your regular benefits.

Instead of being in this research study, your choices may include getting treatment or care for your cancer without being in a study or taking part in another study. These alternative treatments have risks and benefits that may be the same or different than those in this research study. Alternative choices are:

- Brigatinib or other ALK inhibitor without being in the study
- Platinum-based chemotherapy

- Radiation
- Surgery

The study doctor can discuss these alternative treatments, including their risks and benefits, with you.

You may choose not to have treatment for cancer at all. If you decide that you don't want any more active treatment, one of your options is called "comfort care." Comfort care includes pain medication and other support. It aims to maintain your comfort and dignity rather than cure disease. Usually, this care can be provided at home. If you think you might prefer comfort care, please discuss this with your family, friends and your doctor.

In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

Detailed Information

The following is more detailed information about this study in addition to the information listed above.

Who can I talk to if I have questions or concerns?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at 713-792-3428 (office) or 713-792-2121 (24 hours).

This research has been reviewed and approved by an Institutional Review Board (IRB – an ethics committee that reviews research studies). If you have questions about your rights as a research subject or if you have questions, concerns, or complaints about the research, you may contact:

WCG IRB
Telephone: 855-818-2289
E-mail: clientcare@wcglinical.com

WCG IRB is a group of people who perform independent review of research.

WCG IRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WCG IRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.
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How many people will be in this study?

About 168 people will be enrolled in the entire study at all locations.

What happens if I agree to be in this research?

Screening Tests
Signing this consent form does not mean that you will be able to take part in this study. The following screening tests will help the doctor decide if you are eligible:

- You will have a physical exam.
- Blood (about 4 tablespoons) will be drawn for routine tests.
- You will have an EKG to check your heart function.
- Tumor tissue leftover from a previous procedure will be collected and used to see if you have a mutation in the ALK gene. If you do not have leftover tissue available, you will have an image-guided tumor biopsy.
    - To perform an image-guided biopsy, a needle is inserted into the affected area using imaging such as CT, ultrasound, or MRI to collect cells or tissue from the tumor. The doctor will use the imaging to guide the needle into the area. Two (2) types of samples may be collected. It will either be a fine needle aspirate (FNA) that collects cells and/or a core biopsy that collects a small piece of tissue.
- You will have a CT or CT/PET scan and MRI scan to check the status of the disease.
- If you can become pregnant, blood (about 1 teaspoon) or urine will be collected for a pregnancy test.

The study doctor will discuss the screening test results with you. If the screening tests show that you are not eligible to take part in the study, you will not be enrolled. Other treatment options will be discussed with you.

Study Groups
If you are found to be eligible to take part in this study, you will receive brigatinib for the first 12 weeks. This is called the induction period. Afterward, if your disease has not progressed (gotten worse), you will be randomly assigned (as in a roll of dice) to 1 of 3 study groups (33% chance of being assigned to 1 of 3 study groups). This is done because no one knows if one study group is better, the same, or worse than the other group.

- If you are in **Group 1**, you will receive brigatinib alone.
- If you are in **Group 2**, you will receive brigatinib plus carboplatin and pemetrexed for 4 cycles followed by maintenance brigatinib and pemetrexed.
- If you are in **Group 3**, you will receive brigatinib plus local consolidation therapy (LCT).

Study Drug Administration
Each cycle is 21 days.

You will receive brigatinib by mouth daily for 12 weeks during the induction period.

- Brigatinib may be taken with or without food.
- Brigatinib tablets should be swallowed whole. Do not crush or chew the tablets.
- You will be given a dosing diary to write down when you take each dose of brigatinib, including if you miss or vomit any doses. Bring the diary with you to each visit, along with any leftover study drug and/or study drug bottles.
- After 12 weeks, if the disease has not progressed, you will continue treatment as described below.

If you are in **Group 1**, you will continue to take brigatinib daily until there is evidence of disease progression, you experience unacceptable side effects as assessed by the study doctor, or you withdraw your consent, whichever occurs first.

If you are in **Group 2**, you will continue to take brigatinib and you will receive pemetrexed by vein over about 10 minutes on Day 1 of Cycles 1-4. You will also receive carboplatin by vein over about 15-60 minutes after pemetrexed on Day 1 of Cycles 1-4. After Cycle 4, you will receive pemetrexed by vein over about 10 minutes every 21 days.

- You will be given standard drugs to help decrease the risk of side effects. You may ask the study staff for information about how the drugs are given and their risks.

If you are in **Group 3**, you will continue to take brigatinib, and the choice of LCT will be discussed with you.

Study Visits
On Day 1 of Cycle 1:
- You will have a physical exam.
- Blood (about 1 ½ tablespoons) will be drawn for routine tests.
- If you can become pregnant, blood (about 1 teaspoon) or urine will be collected for a pregnancy test.

On Day 8 of Cycle 1:
- You will have a physical exam.
- Blood (about 1 ½ tablespoons) will be drawn for routine tests.

Every 6 weeks during the induction period:
- You will have a physical exam.
- Blood (about 1 ½ tablespoons) will be drawn for routine tests.
- You will have an EKG to check your heart function.
- You will have a CT or CT/PET scan and MRI scan to check the status of the disease.

Every 12 weeks after the induction period:

- You will have a physical exam.
- Blood (about 1 ½ tablespoons) will be drawn for routine tests.
- If you can become pregnant, blood (about 1 teaspoon) or urine will be collected for a pregnancy test.
- You will have a CT or CT/PET scan and MRI scan to check the status of the disease.

End-of-Dosing Visit

At the end of treatment (within 2 weeks of the last dose of the study drug):

- You will have a physical exam.
- Blood (about 1 ½ tablespoons) will be drawn for routine tests.
- You will have an EKG to check your heart function.
- You will have a CT or CT/PET scan and MRI scan to check the status of the disease.
- If you can become pregnant, blood (about 1 teaspoon) or urine will be collected for a pregnancy test.

Follow-Up

About 30 days after the last dose of the study drug:

- You will have a physical exam.
- Blood (about 1 ½ tablespoons) will be drawn for routine tests.

Every 3 months for 2 years after your last dose of brigatinib, you will be called and asked about how you are doing. Each phone call should take about 5-10 minutes.

If you are in **Group 2 or Group 3**, about every 12 weeks for 2 years after your last dose of brigatinib, you will have a CT or CT/PET scan and MRI scan to check the status of the disease.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible for the following:

- Follow study directions, including taking the study drug as directed and completing the dosing diary.
- Come to all study appointments (or contact the study team to reschedule).
- Tell the study team about any symptoms or side effects you have.
- Tell the study doctor/study staff about all medications that you are taking or plan to take, including prescription and over-the-counter medications, supplements, vitamins, and herbal remedies. Talk to your study doctor if you are taking any medications such as ketoconazole, clarithromycin, rifampin, and herbal medication (such as St. John 's Wort) and grapefruit-containing products. These

medications may interact with brigatinib. Other medications may be harmful to take with brigatinib.
- You should not receive other anti-cancer agents (for example, chemotherapy, immunotherapy, biologic therapy, and/or hormone therapy other than for replacement or appetite stimulant) while on treatment in this study.

What happens if I say yes, but I change my mind later?

You can leave the research at any time; it will not be held against you. You may withdraw from participation in this study without any penalty or loss of benefits. If you withdraw from this study, you can still choose to be treated at MD Anderson.

If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor who can help you safely stop study treatment. It may be dangerous to suddenly stop study treatment. The study doctor will also decide if you need to have any visits or tests to check on your health.

If you stop being in the research, already collected data may not be removed from the study database. You may be asked whether the study doctor can collect data from your routine medical care. If you agree, this data will be handled the same as research data.

Is there any way being in this study could be bad for me? (Detailed Risks)

While on this study, you are at risk for side effects. You should discuss these with the study doctor. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after treatment is stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Side effects will vary from person to person, and some may occur after you have stopped receiving treatment. Tell the study staff about any side effects you may have, even if you do not think they are related to the study drugs/procedures.

Brigatinib, carboplatin, and pemetrexed may commonly cause low blood cell counts (red blood cells, platelets, and/or white blood cells):

- A low red blood cell count (anemia) may cause difficulty breathing and/or fatigue. You may need a blood transfusion.
- A low platelet count increases your risk of bleeding (such as nosebleeds, bruising, stroke, and/or digestive system bleeding). You may need a platelet transfusion.
- A low white blood cell count increases your risk of infection (such as pneumonia and/or severe blood infection). Infections may occur anywhere and become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

Brigatinib Side Effects

Common (occurring in more than 20% of patients)

• high blood pressure • fatigue • headache • skin rash • hand-foot syndrome (palms of hands/soles of feet having pain, swelling, and blistering) • abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood pressure, organ failure, heart problems, changes in mental status, and/or seizure)	• high blood sugar (possible diabetes) • abdominal pain • diarrhea • abnormal digestive blood test (possible inflammation of the pancreas) • nausea • vomiting	• low blood cell counts (red, white) • abnormal liver test (possible liver damage) • back pain • muscle damage and/or muscle breakdown • muscle pain • abnormal kidney test (possible kidney damage) • cough • difficulty breathing

Occasional (occurring in 3-20% of patients)

• slow heartbeat • swelling • difficulty sleeping • itching • skin sensitivity to sunlight or lamps • dry skin • constipation • loss of appetite • mouth blisters/sores (possible difficulty swallowing) • upset stomach • low blood cell counts (platelets)	• increased risk of bleeding • dizziness • nerve damage (possible numbness, pain, and/or loss of motor function) • joint pain • muscle spasms • blurry vision • cataracts (clouding of the lens of the eye) • double vision • increased pressure in the eye (possible vision loss)	• swelling under the central part of the retina (possible vision loss) • swelling of the eye nerve (possible vision loss) • lung inflammation (possible difficulty breathing) • low oxygen level in the blood (possible lightheadedness) • fever • pain

Frequency Unknown

• tissue swelling	• abnormal taste	• allergic reaction

Rarely (in fewer than 3% of patients) the drug may cause severe weakness.

Carboplatin Side Effects

Common (occurring in more than 20% of patients)

• abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood pressure, organ failure, heart problems, changes in mental status, and/or seizure)	• vomiting • low blood counts (red/white/platelets) • pain	• abnormal liver tests (possible liver damage) • abnormal kidney test (possible kidney damage)

Occasional (occurring in 3-20% of patients)

• nerve damage (possible numbness, pain, and/or loss of motor function) • hair loss (partial or total)	• abdominal pain • nausea • constipation • diarrhea	• weakness • abnormal liver tests (possible yellowing of the skin and/or eyes) • allergic reaction • infection

Rare but serious (occurring in fewer than 3% of patients)

• high blood pressure • low blood pressure (possible dizziness/fainting) • heart failure • stroke • dehydration • blood vessel blockage	• destruction of red blood cells (possible anemia, kidney damage, and/or failure) • reduced blood supply to the arms and legs • blindness • hearing loss	• difficulty breathing due to narrowing of the airways • tissue death at the injection site caused by drug leakage • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure)

It is not known how often the following side effects may occur:

• decreased bone marrow function

Pemetrexed Side Effects

Common (occurring in more than 20% of patients)

• fatigue	• nausea	• loss of appetite

Occasional (occurring in 3-20% of patients)

• swelling • fever • nerve damage (possibly affecting movement and/or causing loss of sensory function) • skin rash and/or peeling • itching • hair loss (partial or total) • allergic skin reaction	• vomiting • mouth blisters/sores (possible difficulty swallowing) • diarrhea • constipation • abdominal pain • low blood cell counts (red, white, platelets) • abnormal liver tests (possible liver damage)	• sore throat • allergic reaction that may be life-threatening (such as difficulty breathing, low blood pressure, and/or organ failure) • infection • painful red, dry, and/or teary eyes (possible eyelid swelling)

Rare but serious (occurring in fewer than 3% of patients)

• fainting • fast heartbeat • severe sunburn-like rash at site of previous radiation (called radiation recall) • blisters • intestinal blockage	• anemia due to destruction of red blood cells • inflammation of the pancreas (possible abdominal pain) • very severe blistering skin disease (loss of large portion of skin and/or ulcers of the skin and digestive tract)	• kidney failure • lung inflammation (possible difficulty breathing) • blockage in the lung (possible pain, shortness of breath, and/or failure to breathe)

Study Drug Combination Side Effects

Using the study drugs together may cause side effects that are not seen when each is given alone. The study drug combination may also increase the frequency and/or severity of the side effects listed above.

General Risks of Stereotactic Radiation Therapy

- Fatigue (feeling tired)
- Weakness
- Skin changes (such as skin peeling, blisters, itching, and/or redness)
- Hair loss (partial or total)
- Chest pain, swelling, and/or color changes
- Change in appearance of the area being radiated
- Low blood cell counts (including red blood cells, white blood cells, and/or platelets)
    - A low red blood cell count (anemia) may cause difficulty breathing and/or fatigue. You may need a blood transfusion.
    - A low platelet count increases your risk of bleeding (such as nosebleeds, bruising, stroke, and/or digestive system bleeding). You may need a platelet transfusion.
    - A low white blood cell count increases your risk of infection (such as pneumonia and/or severe blood infection). Infections may occur anywhere and become life-threatening. Symptoms of infection may include fever, pain, redness, and/or difficulty breathing.
- Sore throat
- Swallowing problems
- Loss of appetite
- Cough
- Difficulty breathing/shortness of breath
- Radiation pneumonitis (inflammation of the lungs caused by radiation treatment to the chest)

Risks of General Surgery:

- Shock, low blood pressure
- Bleeding
- Wound infection
- Deep vein thrombosis, clots
- Lung complications including difficulty breathing
- Urine retention that is usually temporary
- Pain
- Muscle weakness
- Nerve injury

General anesthesia

The common side effects of general anesthesia include nausea and vomiting, dry mouth, sore throat or hoarseness, chills, confusion, dizziness, muscle aches, itching and difficulty urinating. Serious, life threatening side effects such as heart rhythm disturbances, strokes or accidents causing brain damage can occur.

Specific risks regarding surgery and general anesthesia may vary based on disease severity and other medical conditions you may have and the particular type of surgery recommended. Please discuss these issues with your physician.

You may be given an addendum for your informed consent for radiation therapy and/or surgery.

Other Risks

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

Having **biopsies** performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site of the biopsies. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site.

EKGs may cause discomfort while lying on the exam table, and the tape on the EKG pads may cause skin irritation.

During the **MRI**, 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 you if you have certain types of metal in your body (as might be found in pacemakers, neurostimulators, or certain clips). It may cause problems with devices, such as pacemakers. If you have metal in your body or devices such as a pacemaker, you should discuss this with the study doctor.

CT scans send x-rays through the body at many different angles. You will be exposed to a small dose of radiation. All radiation adds up over a lifetime and may increase the risk of new cancer forming. Some people may feel “closed in” while lying in the scanner. However, the scanner is open at both ends, and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or radiology technicians will give comfort, or the scanning will be stopped. Solution may also be given by vein to make the x-ray pictures more accurate. This may cause an uncomfortable feeling of warmth, nausea, and/or severe allergic reactions. The solution injection may also cause pain, bleeding, bruising, hives, and/or itching.

A **PET scan** may cause you to feel “closed in” while lying in the scanner. However, the scanner is open at both ends and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or technicians will give comfort or the scanning will be stopped.

The PET scan exposes your body to radiation. The radioactive solution does not remain in your system for a long period of time. However, you should wait 2 hours before holding an infant or getting close to a pregnant woman to avoid exposing them to radiation. You should drink fluids after the scan to help remove the solution from your system.

Although every effort will be made to keep study data safe, there is a chance that your personal health information could be lost or stolen, which may result in a **loss of confidentiality**. All study data will be stored in password-protected computers and/or locked file cabinets and will continue to be stored securely after the study.

In addition to these risks, this research may hurt you in ways that are unknown. These may be a minor inconvenience or may be so severe as to cause death.

You will be told about any new information that may affect your health, welfare, or choice to stay in the research.

Pregnancy Related Risks

Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant, breastfeed a baby, or father a child while on this study. You must use birth control during the study and for 3 months (for males) or 4 months (for females) after the end of study treatment if you are sexually active.

Brigatinib may decrease the effectiveness of hormonal birth control. Therefore, women are recommended to use non-hormonal methods of birth control during treatment with brigatinib and for at least 4 months after the last dose.

Birth Control Specifications
For females:

- Sexual abstinence (no sexual intercourse)
- Intrauterine device (IUD) or intrauterine system (IUS)
- Bilateral tubal ligation (both tubes tied)
- Vasectomized partner

For males:

- Sexual abstinence (no sexual intercourse)
- Vasectomy (removal of the tube that carries sperm from the testicle to the penis)
- Female partner(s) utilizing highly effective method of birth control

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away.

Getting pregnant will result in your removal from this study.

Males: Tell the doctor right away if your partner becomes pregnant or suspects pregnancy.

Will it cost anything to be in this study? Will I be paid to be in this study?

You and/or your insurance provider will be responsible for the costs of brigatinib, carboplatin and pemetrexed (if you receive them), and/or local consolidation therapy (if you receive it).

You and/or your insurance provider will not have to pay for certain research exams and procedures done that are covered by the study.

You and/or your insurance provider will be responsible for the costs of routine clinical services (such as diagnostic/therapeutic procedures, drugs, devices, laboratory assays, and other services that would ordinarily be ordered for medical care, regardless of whether or not you are participating in a study). There may be extra costs that are not covered by your medical plan that you will have to pay yourself.

Taking part in this study may result in added costs to you (such as transportation, parking, meals, or unpaid leave from work). You may have to pay for medication prescribed to treat or prevent side effects, and you may have to visit the clinic/hospital more often than if you were not participating in this study.

If you have insurance, talk to your insurance provider and make sure that you understand what your insurance pays for and what it does not pay for if you take part in this study. Also, find out if you need approval from your plan before you can take part in the study.

You may ask that a financial counselor be made available to you to talk about the costs of this study.

You will not receive any compensation for taking part in this study.

There are no plans to compensate you for any products developed from this research.

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who need to review this information. Complete secrecy cannot be promised. Organizations that may inspect and copy your information include the IRB and other representatives of this organization.

Any personal information that could identify you will be removed or changed before data are shared with other researchers or results are made public.

The sponsor, monitors, auditors, the IRB, and the Food and Drug Administration will be granted direct access to your medical records to conduct and oversee the research. By signing this document, you are authorizing this access. The results of this research may be published. However, your name and other identifying information will be kept confidential.

Federal law provides additional protections of your medical records and related health information. These are described below.

Will my data or samples be used for future research?

Your personal information and/or samples are being collected as part of this study. These data and/or samples may be used by researchers at MD Anderson and Takeda or shared with other researchers and/or institutions for use in future research.

In some cases, all of your identifying information may not be removed before your data or research samples are used for future research. If future research is performed at MD Anderson, the researchers must get approval from the MD Anderson IRB before your data and/or research samples can be used. At that time, the IRB will decide whether or not further permission from you is required. If this research is not performed at MD Anderson, MD Anderson will not have oversight of any data and/or samples.

If identifiers are removed from your identifiable private information or identifiable samples that are collected during this research, that information or those samples could be used for future research studies or shared with another researcher for future research studies without your additional informed consent.

Some of your specimens and genetic and/or health information might also be placed into one or more external publicly-accessible scientific databases. Your name and other information that could directly identify you (such as your address or social security number) will never be placed into these external databases. A researcher who wants to study information from these databases must have an approved study and work with the group overseeing the database to obtain the information.

Can I be removed from the research study without my permission?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include:

- It is in your best interest.
- You have a side effect that requires stopping the research.
- You become pregnant.
- The research is stopped by the FDA or the sponsor.
- You are unable to take the study drugs.
- You are unable to keep your scheduled appointments or follow the study directions.

What happens if I get hurt from being in this study?

If you get sick or hurt and it is related to your participation in this study, you will be given care at MD Anderson (if you are at the clinic when you are sick or hurt). If you get hurt or sick and you are not at the clinic (for example, you are at home or at another doctor's office):

- call your personal doctor right away (or in an emergency, call 911)
- tell your personal doctor or ER staff that you are in this study (try to give them a copy of this consent form or show them your participant card)
- call the study doctor (Dr. Yasir Elamin, at 713-792-3428) or 713-792-2121 (24 hours)

The sponsor may pay for the treatment you received because you were hurt or sick during the study. MD Anderson does not know at this time what you may be reimbursed for. A financial counselor will be made available to you after the injury or illness is reported. If the sponsor pays any of your medical expenses, they may need to be given your name, date of birth, and Medicare ID or social security number.

You may also contact the MD Anderson IRB at 713-792-6477 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

What else do I need to know?

This research is being funded by Takeda.

MD Anderson may benefit from your participation and/or what is learned in this study.

Your information and samples (both identifiable and de-identified) may be used to create products or to deliver services, including some that may be sold and/or make money for others. If this happens, there are no plans to tell you, or to pay you, or to give any compensation to you or your family.

Most tests done on samples in research studies are only for research and have no clear meaning for health care. If the research with your identifiable information or samples gives results that do have meaning for your health, the researchers will not contact you to let you know what they have found.

This research study involves genetic testing. The Genetic Information Nondiscrimination Act (GINA) prohibits health insurers or health plan administrators from requesting or requiring genetic information of you or your family members, or using such information for decisions regarding your eligibility for insurance or your premiums. However, this law does not provide the same protection for disability, life insurance, or long-term care insurance. GINA also prohibits most employers (with 15 employees or more) from using genetic information when making decisions on your employment, including decisions related to hiring, firing, promotion, pay, and job assignments. Please contact the study doctor if you would like more information about GINA and how it protects you from genetic discrimination.

This research study involves genetic testing, which may include whole genome sequencing. Whole genome sequencing is a type of testing in which researchers study your entire genetic makeup (DNA). This may help researchers learn how changes in the ordering of genes may affect a disease or response to treatment. If genetic research is done with your samples, those who have access to those samples may be able to identify you. The results of this research may also be able to be linked to you.

Optional Procedures for the Study

You do not have to agree to the optional procedures in order to take part in this study. There are no benefits to you for taking part in the optional procedures. Future patients may benefit from what is learned. You may stop taking part at any time. There will be no cost to you for taking part in the optional procedures.

Optional Procedure #1: Tumor Tissue Samples
If you agree, tumor tissue leftover from a previous procedure will be collected and used for research purposes. This includes genetic testing and biomarker analysis. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drug.

If you do not have leftover tissue available, you will have a tumor biopsy at baseline and/or disease progression.

Optional Procedure #2: Blood Samples
If you agree, blood samples (up to about 4 tablespoons) will be collected at baseline, randomization, and disease progression (if it occurs) for research purposes. This includes biomarker analysis.

Optional Procedure Risks: Please see the Detailed Risks section for the risks of biopsies and blood collections.

CONSENT/PERMISSION/AUTHORIZATION FOR OPTIONAL PROCEDURES
Circle your choice of "yes" or "no" for each of the following optional procedures:

Optional Procedure #1: Do you agree to have tumor tissue collected (archival or fresh biopsy) at baseline and/or disease progression for research purposes?

YES NO

Optional Procedure #2: Do you agree to have blood collected at baseline, randomization, and disease progression (if it occurs) for research purposes?

YES NO

Authorization for Use and Disclosure of Protected Health Information (PHI):

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:

- Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
- WCG IRB
- Takeda, who is a sponsor or supporter of this study, and/or any future sponsors/supporters of the study, and/or licensees of the study technology
- Study monitors and auditors who verify the accuracy of the information
- Individuals who put all the study information together in report form

Study sponsors and/or supporters receive limited amounts of PHI. They may also view additional PHI in study records during the monitoring process. MD Anderson's contracts require sponsors/supporters to protect this information and limit how they may use it.

The results of this research may be published in scientific journals or presented at medical meetings, but your identity will not be disclosed.

B. Signing this consent and authorization form is optional but you cannot take part in this study or receive study-related treatment if you do not agree and sign.

C. MD Anderson will do its best to protect the privacy of your records, but it is possible that once information is shared with people listed on this form, it may be released to others. If this happens, your information may no longer be protected by federal law and it may be re-disclosed.

D. The permission to use your PHI will continue indefinitely unless you withdraw your authorization in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP) or you may contact the Chief Privacy Officer at 713-745-6636. If you withdraw your authorization, you will be removed from the study and the data collected about you up to that point can be used and included in data analysis. However, no further information about you will be collected.

E. 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.

CONSENT/AUTHORIZATION

I understand the information in this consent form. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

WITNESS TO CONSENT
I was present during the explanation of the research to be performed under this protocol.

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE
A witness signature is only required for non-English speakers utilizing the short form consent process (VTPS) and patients who are illiterate.

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

PERSON OBTAINING CONSENT
I have discussed this research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

_____ _____
SIGNATURE OF PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT