THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

A Phase-2, Two-Cohort Trial of Neoadjuvant nab-Paclitaxel and Alpelisib in Anthracycline Refractory Triple Negative Breast Cancer with PIK3CA or PTEN alterations
2019-0752

Study Chair: Senthil Damodaran

_____ _____
Participant's Name Medical Record Number

This is an informed consent and authorization form for a research study. It includes a summary about the study. A more detailed description of procedures and risks is provided after the summary.

STUDY SUMMARY

The goal of this clinical research study is to learn if the combination of alpelisib and nab-paclitaxel can help to control triple-negative breast cancer (TNBC) by shrinking the tumors in the breast and/or lymph nodes before they are surgically removed. The safety of this treatment combination will also be studied.

This is an investigational study. Nab-paclitaxel is FDA approved for use in breast cancer that is advanced or metastatic (has spread to other parts of the body). Alpelisib is FDA approved and commercially available for use in breast cancer with mutations (genetic changes) in the ER+/HER2-, and PIK3CA genes. The combination of these drugs is not FDA approved or commercially available. At this time, it is being used in research only. The study doctor can explain how these study drugs are designed to work.

Treatment with the study drugs may help to shrink the size of the tumor(s) before surgery. Future patients may benefit from what is learned. There may be no benefits for you in this study.

Your participation is completely voluntary. 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. If you take part in this study, you may experience high blood sugar while receiving treatment, which may require

medical care. This is the first time this combination has been offered to patients with your disease type and tumor mutation (genetic change) type.

You can read a list of potential side effects below in the Possible Risks section of this consent.

You will receive alpelisib for up to 4 cycles (84 days total) of the study drugs and may be on study for up to about 16 weeks.

Alpelisib will be provided at no cost to you while you are on study. You and/or your insurance provider will be responsible for the cost of nab-paclitaxel.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive standard chemotherapy (such as paclitaxel) or surgery. You may choose to receive other investigational therapy, if available. You may choose not to have treatment for cancer at all. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

1. STUDY DETAILS

Screening Tests

Signing this consent 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 2 teaspoons) will be drawn for routine tests and tests to measure your fasting level of blood sugar and cholesterol (fat in the blood). Whenever you have a fasting blood draw scheduled on this study, you should not eat and drink only water starting at midnight the night before your scheduled blood draw.
- Depending on your tumor type, blood (about 1 teaspoon) may be drawn to look for circulating tumor DNA (ctDNA). ctDNA is the genetic material from tumor cells in your blood.
- Urine will be collected for routine tests. If you can become pregnant, this sample will also be used for a pregnancy test. To take part in this study, you must not be pregnant.
- You will have imaging scans (either MRI or ultrasound) of the breast and lymph nodes to check the status of the disease.

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 this study, you will not be enrolled. Other treatment options will be discussed with you.

Up to 62 participants will be enrolled in this study. All will take part at MD Anderson.

Study Drug Administration

Each study cycle is 21 days.

If you are found to be eligible for this study, you will take **alpelisib** by mouth every day for 4 cycles.

On Days 1, 8, and 15 of each cycle, you will also receive **nab-paclitaxel** by vein over about 30 minutes.

If you have side effects, the study doctor will determine which drug caused the side effect. The study doctor may decide to lower the dose level of one or both drugs, or may decide that you will need to stop taking the drug(s) for a short time. If your dosing is stopped, you may be able to restart the study drug(s) later at the same dose or a lower dose. The study doctor will discuss this with you.

You will no longer be able to take the study drugs if your disease gets worse, if intolerable side effects occur, or if you are unable to follow study directions.

Your participation on the study will be over after the follow-up visit described below.

Study Visits

On **Day 1 of each cycle:**

- You will have a physical exam
- Blood (about 2 teaspoons) will be drawn for routine tests, including a test of your fasting blood sugar and/or cholesterol level.
- During Cycle 1, if you can become pregnant, urine will be collected for a pregnancy test.

On **Days 1, 8, and 15 of Cycles 1 and 2:**

- Blood (about 1 teaspoon) will be drawn to check your fasting blood sugar level.

At the **end of Cycles 2 and 4:**

- You will have imaging scans (either MRI or ultrasound) of the breast and lymph nodes to check the status of the disease.

After Cycle 4, you may then have surgery to remove the tumor(s). You will be given a surgery consent form which describes the procedure and its risks. If you do not have surgery, you may still have a lymph node biopsy or removal, based on standard care. Your doctor can discuss this with you.

Follow-Up

Within 30 days (+/- 10 days) after surgery/biopsy, you will have a follow-up visit. During this visit:

- Blood (about 2 teaspoons) will be drawn for routine tests.
- If you can become pregnant, urine will also be collected for a pregnancy test.
- You will have imaging scans (either MRI or ultrasound) of the breast and lymph nodes to check the status of the disease.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. These side effects will vary from person to person. The more commonly occurring side effects are listed in this form, as are the rare but serious side effects. You should discuss these with the study doctor. You may also want to ask about the uncommon side effects that may have been observed in small numbers of patients but are not listed on 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.

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.

Alpelisib and nab-paclitaxel each may 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.

Alpelisib Side Effects

Common (occurring in more than 20% of patients)

• swelling (arms/legs) • fatigue • high blood sugar (possible diabetes)	• loss of appetite • weight loss • nausea/vomiting • diarrhea	• mouth blisters/sores (possible difficulty swallowing) • low red blood cell count

Occasional (Occurring in 3-20% of patients)

• abnormal EKG • inflammation (swelling and redness) of tissue that lines your organs • high blood pressure • headache • fever • dizziness • anxiety • depression • difficulty sleeping • dehydration • skin rash/dryness • hair loss (partial or total)	• 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) • abnormal taste • constipation • upset stomach	• abdominal pain • low blood cell count (platelet/white) • abnormal liver tests (possible liver damage) • muscle spasms • blurry vision • dry eyes • abnormal kidney test (possible kidney damage) • difficulty breathing

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

• swelling around the eyes • very severe blistering skin disease (with ulcers of the skin and digestive tract) • fingernail loss	• abnormal pancreas test (possible pancreas damage) • inflammation of the pancreas (possible abdominal pain) • kidney failure	• lung inflammation (possible difficulty breathing) • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure)

If you experience any new or changing respiratory symptoms such as new or worsening cough, wheezing, feeling short of breath or difficulty breathing, you should contact your study doctor right away.

Some patients who have received Alpelisib have had lung inflammation (pneumonitis) that resulted in death.

<u>Nab-Paclitaxel Side Effects</u>

Common (occurring in more than 20% of patients)

• abnormal EKG • swelling • fatigue • fever • nerve damage (possible numbness, pain, and/or loss of sensory/motor function)	• hair loss (partial or total) • skin rash • nausea/vomiting • diarrhea • dehydration • loss of appetite	• abnormal liver tests (possible liver damage and/or yellowing of the skin and/or eyes) • weakness • pain • infection

	• low blood cell counts (red, white, platelets)	

Occasional (occurring in 3-20% of patients)

• low blood pressure (possible dizziness/fainting) • high blood pressure • chest pain • heart failure • sudden stopping of the heart • fast heartbeat • flushing • yellowing of the skin and/or eyes • blood clots in a vein (possible pain, swelling, and/or redness) • headache • depression	• low blood levels of potassium (possible weakness and/or muscle cramps) • constipation • abnormal taste • intestinal blockage • inflammation of the intestines • inflammation of the bile duct • mouth blisters/sores (possible difficulty swallowing) • vision problems • swelling under the central part of the eye (vision loss) • abnormal kidney test (possible kidney damage)	• difficulty breathing • lung inflammation (possible difficulty breathing) • blood clots/blockage in the lung (possible pain, shortness of breath, and/or failure to breathe) • cough • nosebleed • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure) • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)

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

• swelling (face) • irregular/slow heartbeat • decreased blood supply to the heart • heart attack or other severe heart problems • stroke and/or temporary stroke symptoms • paralysis of nerves controlling the head and neck • decreased brain function due to liver damage • difficulty walking • difficulty spelling	• sweating/night sweats • small bleedings in your skin due to blood clots • severe sunburn-like rash at site of previous radiation (called radiation recall) • bruising • low blood levels of phosphate (possible bone damage) • low blood levels of albumin (possible swelling, weakness, and/or fatigue) • low blood levels of	• painful and/or frequent urination • blood in the urine • loss of bladder control • decreased blood flow to part of the bowel (possibly causing tissue death) • paralysis of the intestines • liver damage and/or failure • decreased/lack of reflexes • involuntary movements • nerve pain • blurry vision

• fainting • dizziness • shaking • restlessness • fingernail pain/discomfort • loss of fingernails • hives • skin sores • very severe blistering skin disease (loss of large portion of skin and/or ulcers of the skin and digestive tract) • hand-foot syndrome (palms of hands/soles of feet having pain, swelling, and blistering) • red skin from sunlight • skin discoloration (including white spots on the skin)	• calcium (possible weakness and/or cramping) • low blood levels of sodium (possible headache, confusion, seizures, and/or coma) • low blood sugar • high blood sugar (possible diabetes) • inflammation of the pancreas (possible abdominal pain) • hole in the intestines (possibly leaking contents into the abdomen) • increased thirst • gas • stomach cramps • painful/sore gums • rectal bleeding	• irritated/red/itchy eyes • double vision • damage to an eye nerve • collapsed lung (possible difficulty breathing) • pain (ear/skin/breasts) • ringing in the ears • lung damage at the site of prior radiation • paralysis of the vocal cords • runny nose • dry nose • pain/swelling of the nose • pain at the site of the tumor/tumor death • skin infections • infection due to the catheter line

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.

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.

Fasting may cause your blood sugar to drop. You may feel tired, hungry, and/or nauseous. If you have diabetes, it is important to talk to your doctor about managing your blood sugar while fasting.

This study may involve unpredictable risks to the participants.

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 at least 12 weeks after your last dose of the study drugs, if you are sexually active.

Highly-effective methods of birth control that are allowed on this study include a combination of any 2 of the following:

- An intrauterine device or system (IUD/IUS)
- Barrier methods of birth control, such as a condom or occlusive cap (diaphragm or cervical/vault cap) PLUS spermicide (foam/gel/film/cream/vaginal suppository)
- Confirmed surgical sterilization by 1 or both partners

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

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.

3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson or Novartis for this injury. You may also contact the Chair of MD Anderson's 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.

Certain tests, procedures, and/or drugs that you may receive as part of this study may be without cost to you because they are for research purposes only. However, your insurance provider and/or you may be financially responsible for the cost of care and treatment of any complications resulting from the research tests, procedures, and/or drugs. Standard medical care that you receive under this research study will be billed to your insurance provider and/or you in the ordinary manner. Before taking part in this study, you may ask about which parts of the research-related care may be provided without charge, which costs your insurance provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this study.

Samples that are collected from you in this study may be used for the development of treatments, devices, new drugs, or patentable procedures that may result in commercial profit.

There are no plans to compensate you for any patents or discoveries that may result from your participation in this research.

You will receive no compensation for taking part in this study.

Additional Information

4. You may ask the study chair (Dr. Senthil Damodaran, at 713-792-2817) any questions you have about this study. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-6477 with any questions that have to do with this study or your rights as a study participant.

5. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. 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. If you withdraw from this study, you can still choose to be treated at MD Anderson.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, Institutional Moon Shots Program, Novartis, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson.

7. You will be informed of any new findings or information that might affect your willingness to continue taking part in the study, and you may be asked to sign another informed consent and authorization form stating your continued willingness to participate in this study.

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

9. This study is supported by: Novartis.

10. In a medical emergency, you may be cared for by someone who has a financial interest with the study sponsor(s)/supporter. If you have any questions about this, you may call the IRB at 713-792-6477.

Future Research

Data

Your personal information is being collected as part of this study. These data may be used by researchers at MD Anderson and Novartis and its authorized agents, and/or shared with other researchers and/or institutions for use in future research.

Samples

Samples (such as blood and/or tissue) are being collected from you as part of this study. Researchers at MD Anderson may use any leftover samples that are stored at MD Anderson in future research.

Before being used or shared for future research, every effort will be made to remove your identifying information from any data and/or research samples. If all identifying

information is removed, you will not be asked for additional permission before future research is performed.

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 Institutional Review Board (IRB) of MD Anderson 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. The IRB is a committee of doctors, researchers, and community members that is responsible for protecting study participants and making sure all research is safe and ethical.

If this research is not performed at MD Anderson, MD Anderson will not have oversight of any data and/or samples.

Genetic Research
Research samples collected from you as part of this study will be used for genetic research, 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.

Conflict of Interest

Dr. Debasish Tripathy (Department Chair and Study Co-Chair) has received compensation from Novartis (the study sponsor) as a Scientific/Advisory Committee Member. The amount received was within the limits of the conflict of interest policy.

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)
   - The IRB and officials of MD Anderson
   - Novartis, who is the supporter of this study, and/or any future supporters of the study
   - Novartis' authorized agents
   - Governmental agencies in other countries where the study drug may be considered for approval
   - 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.

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 keep your PHI confidential when possible (according to state and federal law). However, in some situations, the FDA could be required to reveal the names of participants.

Once disclosed outside of MD Anderson, federal privacy laws may no longer protect your PHI.

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

LEGALLY AUTHORIZED REPRESENTATIVE (LAR)

The following signature line should only be filled out when the participant does not have the capacity to legally consent to take part in the study and/or sign this document on his or her own behalf.

_____ _____
SIGNATURE OF LAR DATE

_____
PRINTED NAME and RELATIONSHIP TO PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under Protocol 2019-0752.

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE

A witness signature is only required for vulnerable adult participants. If witnessing the assent of a pediatric participant, leave this line blank and sign on the witness to assent page instead.

_____
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.

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT

TRANSLATOR

I have translated the above informed consent as written (without additions or subtractions) into_____and assisted the people
(Name of Language)
obtaining and providing consent by translating all questions and responses during the consent process for this participant.

_____ _____ _____
NAME OF TRANSLATOR SIGNATURE OF TRANSLATOR DATE

☐ Please check here if the translator was a member of the research team. (If checked, a witness, other than the translator, must sign the witness line below.)

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL TRANSLATION DATE
(OTHER THAN TRANSLATOR, PARENT/GUARDIAN,
OR STUDY CHAIR)

_____
PRINTED NAME OF WITNESS TO THE VERBAL TRANSLATION