Official Title: LCI-BRE-H2N-PEPP-001: A Pilot Study of Paclitaxel Plus Pembrolizumab in Patients with Metastatic HER2-Negative Breast Cancer
NCT03018080
IRB-Approved Date: 6/9/2021

ATRIUM HEALTH
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Sponsor / Study Title:	**Levine Cancer Institute/ A Pilot Study of Paclitaxel Plus Pembrolizumab in Patients with Metastatic HER2-Negative Breast Cancer**
Protocol Number:	**LCI-BRE-H2N-PEPP-001**
Principal Investigator:	**Antoinette Tan, MD**
Telephone:	[redacted] **(24 Hours)** [redacted] **(24 Hours)**
Address:	**Levine Cancer Institute** [redacted]

INTRODUCTION

Dr. Antoinette Tan and her associates (the investigators) are asking you to participate in a research study at Levine Cancer Institute (LCI) and Atrium Health (AH). The purpose of this study is to determine if the research study drug, pembrolizumab, in combination with chemotherapy, is successful at treating metastatic breast cancer and if it is safe. You are being asked to take part in this study because you have been diagnosed with metastatic breast cancer.

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You have also been told that you have the option not to participate. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask your study doctor for more explanation.

This study is being carried out under the sponsorship of Levine Cancer Institute (LCI). Merck is the pharmaceutical company that makes the research drug, pembrolizumab, which will be used in this study.

WHY IS THIS STUDY BEING DONE?

This is a research study to determine if the study drug, pembrolizumab (KEYTRUDA), is safe to use in combination with a chemotherapy drug called paclitaxel. Other goals in this study are to learn about the effect of combining paclitaxel and pembrolizumab on tumor growth, and to understand if there is a difference when giving paclitaxel and pembrolizumab on different study treatment schedules.

We will compare giving the chemotherapy paclitaxel alone for 2 cycles (6 weeks) followed by giving pembrolizumab and paclitaxel during future cycles to giving pembrolizumab and paclitaxel starting with the first cycle. We also want to collect information to learn about DNA (the genetic material in the cells in the body that serve as blueprints for making proteins) and proteins in the blood and tumor that may predict or show an effect of pembrolizumab.

Pembrolizumab has been approved by the Food and Drug Administration (FDA) in the United States to treat several different cancers to include locally recurrent unresectable or metastatic triple negative breast cancer (TNBC) in combination with chemotherapy and whose tumor express PD-L1 as determined by an FDA approved test. Paclitaxel is an FDA-approved anticancer drug. Paclitaxel is a standard chemotherapy used to treat metastatic breast cancer.

Subjects in this study will be randomized to one of the two study treatment schedule groups. Randomized means you have a 50:50 chance, the same as a flip of a coin, of being assigned to either study treatment group. You or your study doctor will not be able to pick which study treatment group you will be in on this study.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

About 40 subjects will take part in this study at Levine Cancer Institute and associated sites. About 20 subjects will be randomized into each of the Cohorts, A and B.

HOW THE STUDY WORKS

Before you begin the study (Baseline):
In order to participate in this study, you will need to review, sign and date this consent form. By doing so, you are giving us permission to determine if you are eligible to participate in this study. To determine if you are eligible, we will need to collect important information from your medical record about your demographics (for example age, race, etc.), medical history, your current disease, any anti-cancer treatments you are receiving or have received before, and any medications you are taking or have recently taken. We will also need to perform some tests, and a complete physical exam to make sure that you are eligible for the study. Some of these tests may need to be repeated if they are done more than 14 days before the first day you receive the study drug(s). We will also need to collect blood for laboratory tests.

If not already done within 28 days before the first day you receive the study drug(s), you will have a scan of the chest, abdomen, and pelvis. The scan will be done using an x-ray machine that uses a computer to take pictures or computerized tomography (CT) scan, or a scan that takes pictures of the body using magnetic waves to look at soft tissue, called magnetic resonance imaging or MRI. We will also ask that you have a bone scan within 28 days of the first day you receive the study drug(s) to determine the presence or absence of disease in your bones at baseline.

A blood or urine pregnancy test will be done for women who can have children, within 14 days of the first day you receive the study drug(s) on this trial.

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The results of the pregnancy test must be negative in order to be in the study. An ECG must also be performed within 14 days of the first day you receive the study drug(s).

We would like to test your tumor for tumor markers or certain types of tumor cells. We will need to collect a fresh tumor biopsy before you receive your first day of study drug(s). However, if your study doctor determines that a new or fresh biopsy is not possible due to difficulty getting to a tumor site or a safety concern, then we may be able to use an archived (previously collected) tumor tissue sample as long as it was collected no more than 12 months prior to this consent being signed. However, if an archived tissue sample is not available, not large enough, or was collected more than 12 months ago, you will not be eligible to participate in this study.

If we are able to collect a fresh tumor sample, we will ask to do a core needle biopsy or a punch biopsy of some of the cancerous tumor. A core needle biopsy is when a needle is inserted into the body from a small surgical cut and into the tumor. The needle is hollow on the inside and removes a small amount of tissue from the tumor. A punch biopsy is when a small round piece of tissue about the size of a pencil eraser is removed using a sharp, hollow, circular instrument. The biopsy will be performed as an outpatient procedure using a local anesthetic.

You may be required to sign a separate non-study related consent that is standard procedure for performing surgical procedures to have the biopsy.

We would also like to collect and test archived tumor tissue samples available from storage. This may include tissue from your first diagnosis and from your diagnosis of metastatic disease. We would like to compare these earlier samples to the samples collected for this study. We would also like to store your archived tissue samples for future, currently unplanned research. We will ask your permission to do this at the end of the consent form.

Blood samples will be collected prior to study treatment initiation, for research purposes to look at certain features in your blood that may be related to your disease. We would also like to test your blood for the BRCA 1 and BRCA 2 mutations if you have not previously been tested for these. The BRCA1 and BRCA2 mutations are changes in the genes that help control a cell's normal growth. If you have not been tested for BRCA 1 and 2 and do not want to be tested for it, you may still be eligible to be in the study.

If you qualify for the study and agree to participate, you will be randomized and enrolled to the study, and we will make arrangements to for you to begin receiving study treatment on the study.

During the study (Intervention; number of visits/cycles):
Cycles on this study are scheduled to last 21 (+/-3) days. You will be scheduled to receive study drug(s) on Days 1 and 8 of each cycle.

The study treatment cohort that you have been assigned will determine the schedule in which you receive the study drug(s).

Cohort A: Phased Regimen
Subjects randomized into cohort A will receive paclitaxel on Days 1 and 8 of each cycle.

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However, they will not receive their first dose of pembrolizumab until Cycle 3 Day 1. Pembrolizumab will be administered on Day 1 of each cycle starting at Cycle 3 and until the final dose of study treatment on study.

Cohort B: Concurrent (at the same time) Regimen
Subjects randomized into cohort B will receive pembrolizumab on Day 1 of each cycle starting with Cycle 1, and paclitaxel on Days 1 and 8 of each cycle. Pembrolizumab will be administered on Day 1 of each cycle and until the final dose of study treatment on study.

In both cohorts, subjects will be given a dose of pre-medication steroids before the paclitaxel (chemotherapy) infusion to prevent possible allergic or hypersensitivity reactions. If you do not have allergic reactions and tolerate the chemotherapy regimen well over time, the investigator may decide to reduce and then remove the steroid pre-medication from the regimen. Also, if a scheduled study treatment of paclitaxel is delayed or missed, you may be rescheduled by your investigator to receive a replacement dose on a later date, within the same cycle. Finally, if you have a side effect to the paclitaxel chemotherapy or if the investigator believes you have received maximum benefit from paclitaxel, he/she may reduce or remove the paclitaxel from your study treatment regimen.

Some assessments will be scheduled to occur on each day that you receive study drug(s) on this study, including vital signs and blood draws. Other assessments and procedures will occur on set intervals. Scans to monitor your disease will occur at least every 6 weeks on this study and may occur less frequently after you have received 6 months of study treatment. Other assessments will occur on specific days and sometimes only on a specific cycle. Several procedures and assessments will occur only on Day 1 of each cycle, including documentation of any changes in medical history, physical exam, and collection of blood to test your liver's function, other organ function, and other blood levels of importance.

We will also schedule an additional biopsy to take a tumor sample as described above ideally from the same site biopsied at baseline (if possible), within 5 days of Cycle 3 Day 1 if your disease can be safely biopsied.

After you complete the intervention (Post-intervention; one visit and follow-up):
After you receive your final dose of study drug(s) on trial, we will schedule an end of study treatment visit to take place within 31 days from the last day of study treatment. We will update any changes in your medical history, perform a physical exam, collect vital signs and blood samples, and review any symptoms you have or have had. You will continue to have scans at the scheduled described above to monitor your disease until your disease worsens or you start new cancer therapy. We will check back with you by phone, in writing, or during clinic visits every 6 months thereafter.

Optional collections
We will also ask if you would be willing to provide additional samples of blood or additional samples of your tumor for additional research. This includes additional blood collections (explained in detail at the end of this consent), and additional tumor biopsies within 5 days of Cycle 5 Day 1 and at the time of disease progression (if your disease progresses). We will further explain the optional tumor biopsies at the end of this consent form.

RISKS

If you decide to take part in this study, study drugs used may cause all, none or some of the following side effects listed. Also, there is always the risk of developing very uncommon or previously unknown side effects. There may be other side effects or risks that are not known at this time. There also is a risk of death.

Pembrolizumab:
Pembrolizumab works by helping your immune system to fight your cancer.
However, pembrolizumab can also cause your immune system to attack normal organs and tissues in your body and can affect the way they work, which can result in side effects. These side effects may be serious (for example, causing hospitalization or be life-threatening), may result in death, and/or may occur after you stop taking pembrolizumab. These side effects can affect more than one of your normal organs and tissues at the same time.

Very common side effects, some may be serious (for example, causing hospitalization, life-threatening or where noted, may cause death); seen in 20% or more of subjects treated with pembrolizumab include the following:

- Diarrhea (loose or watery stools)
- Itching of the skin
- Cough
- Nausea
- Fatigue

Common side effects, some may be serious; seen in 5% to less than 20% of subjects treated with pembrolizumab include the following:

- Joint pain
- Fever
- Back pain
- Rash
- Pain in your belly
- Loss of skin color
- Not enough thyroid hormone so you may feel tired, gain weight, feel cold, and/or have infrequent or hard stools (hypothyroidism)
- Low levels of salt in the blood that may cause you to feel tired, feel confused, have a headache, have muscle cramps, and/or feel sick to your stomach (hyponatremia)

Uncommon side effects, some may be serious; seen in 1% to less than 5% of subjects treated with pembrolizumab include the following:

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- Too much thyroid hormone so you may feel anxious, feel angry, have trouble sleeping, feel weak, tremble, sweat, feel tired, and/or have loose or watery stools (hyperthyroidism)
- Inflammation of the lungs, so you may feel short of breath and cough (pneumonitis)
- Inflammation of the bowels/gut, which may cause severe pain in your belly with loose or watery stools, and black, tarry, sticky stools or stools with blood or mucus (colitis)
- Inflammation of the skin so you may have peeling of the skin, itchiness, and/or skin redness. The skin inflammation (for example, peeling, itching and redness) could also be widespread throughout your body. More severe skin reactions may involve the inside of your mouth, the surface of your eye and genital areas, and/or may cause the top layer of your skin to peel from all over your body which can cause severe infection (Severe skin reactions, including Stevens-Johnson syndrome/or toxic epidermal necrolysis, which may be serious or potentially life-threatening)
- Infusion reaction, where you may feel dizzy or faint, feel flushed, get a rash, have a fever and/or feel short of breath, experience a decrease in your blood pressure at the time of receiving your infusion (IV) or just after, or have pain at the site of infusion.

Rare side effects, some may be serious; seen in less than 1% of subjects treated with pembrolizumab include the following:

- Inflammation of the liver that may make you feel sick to your stomach and vomit, feel like not eating, feel tired, have a mild fever, have a pain in the right side of your belly, yellow eyes and skin, and dark urine (hepatitis)
- Inflammation of the pituitary gland (a gland in the head), which may cause you to feel sick to your stomach or have headaches, changes in your behavior, double vision, few to no menstrual cycles, weakness, vomiting and dizziness, or fainting (hypophysitis)
- Adrenal glands (glands on top of the kidneys) may not make enough hormone, which could cause tiredness, weight loss, muscle weakness, feeling faint, having joint, muscle and belly aches, nausea, vomiting, loose or watery stools, fever, salt craving, and sometimes darkening of the skin like a suntan (adrenal insufficiency)
- Inflammation of the kidney so you may pass less urine or have cloudy or bloody urine, swelling and low back pain (nephritis)
- Inflammation of the muscles so you may feel weak or have pain in the muscles (myositis)
- Inflammation of the pancreas (a gland in your abdomen that controls sugar levels) so you may have severe pain in the top part of your belly that may move to your back, feel sick to your stomach, and have vomiting that gets worse when you eat (pancreatitis)
- Inflammation of the eye so you may have eye redness, blurred vision, sensitivity to light, eye pain, see floaters or have headaches (uveitis)
- Type 1 Diabetes, a condition that can cause too much sugar in your blood, feeling thirstier than usual, frequent urination and weight loss. You are likely to need regular insulin shots
- Inflammation of the nerves that may cause pain, weakness or tingling in your hands and feet, and may spread to your legs, arms and upper body leading to severe muscle weakness and possible temporary paralysis (inability to move) (Guillain-Barré syndrome)
- Inflammation of the middle layer of your heart wall (myocarditis) that may cause your heart to have difficulty pumping blood throughout your body, which can cause chest pain,

shortness of breath and swelling of the legs. You may experience a fast or irregular heartbeat that may cause dizziness or fainting (myocarditis)
- Inflammation of the thyroid gland, an organ that makes and stores thyroid hormones. This condition may lead to change in your heart rate, blood pressure, body temperature, and the rate at which food is converted into energy (thyroiditis)
- A condition that may make you feel weak and tired and may cause drooping of the eyelids, blurred or double vision, difficulty swallowing, slurred speech, weakness in your arms and legs, or difficulty breathing (myasthenic syndrome/myasthenia gravis including exacerbation)
- The formation of small clusters of immune cells (called granulomas) in parts of your body such as your lymph nodes, eyes, skin or lungs (sarcoidosis)
- Inflammation of the brain (encephalitis) with confusion and fever. This may also include: disorientation, memory problems, seizures (fits), changes in personality and behavior, difficulty speaking, weakness or loss of movement in some parts of your body, and loss of consciousness
- Inflammation of the spinal cord (myelitis) with pain, numbness, tingling, or weakness in the arms or legs, bladder or bowel problems including needing to urinate more frequently, urinary incontinence, difficulty urinating, and constipation
- Inflammation of the blood vessels

Additionally, since pembrolizumab was approved in September 2014, the following side effects have been reported by people receiving pembrolizumab. These side effects were voluntarily reported from a group of people of unknown size. It is not possible to estimate the frequency of this side effect:

- Inflammation of the joints which may include joint pain, stiffness and/or swelling (arthritis)
- Severe responses of the immune system that cause the body to attack its own blood cells, spleen, liver, lymph nodes, skin and brain. This may include fever, rash, inflammation of the liver, yellowing of the skin, an enlarged liver and spleen, low blood counts, and enlarged lymph nodes. The nervous system may also be affected and cause confusion, seizures, and even coma (hemophagocytic lymphohistiocytosis)
- Changes in eyesight, eye pain, whitish patches on the skin and hearing loss (Vogt-Koyanagi-Harada syndrome)
- Inflammation and scarring of the bile ducts (tubes that carry digestive fluid that is made in the liver). This can cause symptoms similar to those seen with inflammation of the liver (hepatitis) such as pain in the right side of your belly, yellow eyes and skin, feeling tired, and itching

If you have had an allogeneic stem cell transplant (a procedure in which a person receives blood-forming stem cells from a donor), you may experience graft versus host disease (GvHD), which may include diarrhea, skin rashes, and liver damage, **after receiving pembrolizumab**. Sometimes this condition can lead to death.

If you have had a solid organ transplant (for example, if you have received a kidney or heart transplant), you may experience rejection of the transplanted organ. Your doctor will monitor you

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and should tell you what signs and symptoms you should report depending on the type of organ transplant that you have had.

Paclitaxel:

Paclitaxel is an FDA-approved and standard anticancer drug for the treatment of metastatic breast cancer. Therefore, the risks and side effects of receiving paclitaxel in the treatment of metastatic breast cancer have been studied extensively.

Tell your healthcare provider right away if you have:

- Severe stomach pain
- Severe diarrhea

The most common side effects include:

- Low red blood cell count (anemia) feeling weak or tired
- Hair loss
- Numbness, tingling, or burning in your hands or feet (neuropathy)
- Joint and muscle pain
- Nausea and vomiting
- Hypersensitivity reaction – trouble breathing; sudden swelling of your face, lips, tongue, throat, or trouble swallowing; hives (raised bumps) or rash
- Diarrhea
- Mouth or lip sores (mucositis)
- Infections – if you have a fever (temperature above 100.4°F) or other sign of infection, tell your healthcare provider right away
- Swelling of your hands, face, or feet
- Bleeding events
- Irritation at the injection site
- Low blood pressure (hypotension)

Tell your healthcare provider if you have any side effect that bothers you or that does not go away. These are not all of the possible side effects of paclitaxel. For more information, ask your healthcare provider or pharmacist.

Allergic Reaction Risks

As with taking any drug, there is a risk of allergic reaction. If you have a very serious allergic reaction, you may be at risk of death. Some symptoms of allergic reactions are:

- Rash
- Wheezing and difficulty breathing
- Dizziness and fainting

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- Swelling around the mouth, throat or eyes
- A fast pulse
- Sweating

Please seek treatment immediately and tell the study doctor and study staff if you have any of these symptoms, or any other side effects, during the study.

Other Risks:

Electrocardiogram (ECG) procedure may cause minimal discomforts during the attachment and removal of the ECG leads to and from the skin.

Tumor Biopsy: Having biopsies performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling and/or infection at the site of the biopsy, shortness of breath from lung collapse and rarely, death. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site. Other potential risks will be described to you and discussed with you by physicians who conduct these biopsies.

CT Scan: CT scans are used to create images of internal bones and organs using radiation. The effect of exposure to radiation adds up over a lifetime. The amount of radiation exposure involved in this trial will not be significantly greater than for subjects with your disease who do not take part in the trial.

In rare cases, the contrast solution that may be given for a CT scan may cause an allergic reaction. Severe allergic reactions can be life threatening. CT contrast solution can cause kidney damage, especially if you are diabetic, dehydrated (lost body water) or elderly.

Magnetic Resonance Imaging (MRI): Risks of MRI include claustrophobia, discomfort due to lying still for a prolonged period of time, and other factors which will be described to you and discussed with you at the MRI center.

Blood Drawing Risks: During this study, blood will be drawn from a vein to perform tests that allow your study doctors to see how you are doing. Drawing blood may cause pain where the needle is inserted, and there is a small risk of bruising and/or infection at the place where the needle is inserted. Some people experience dizziness, upset stomach, or fainting when their blood is drawn.

Pregnancy Precautions:

Female:
It is not known if the study drug(s) may affect an unborn or nursing baby. If you are pregnant, trying to become pregnant or breast-feeding, you may not be in the study. The study doctor will perform a blood or urine pregnancy test before the start of the study, if you are able to have a baby.

If you are able to have a baby, you must avoid having sex (abstinence) or use reliable birth control methods during the study and for a period of 120 days after your last dose of study drug. If you

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become pregnant during the study you must notify the study doctor right away. The study drugs will be stopped and you will be taken out of the study.

Male:
There may be risks if you are male and your partner is pregnant or trying to become pregnant. If you are male and your partner is able to have a baby, you and your partner must avoid having sex (abstinence) or use reliable birth control methods during the study and for a period of 120 days after your last dose of study drug pembrolizumab.

If your partner becomes pregnant during the study, you must notify the study doctor right away. If your partner is already pregnant when you begin the study, you must use a condom (male) during the study and for a period of 120 days after your last dose of pembrolizumab. You must also agree to not donate sperm during the study and for a period of 120 days after your last dose of study drug.

Male and Female:
The following birth control methods for subjects who are able to conceive a child or a subject's partner are allowed during the study as per local regulations or guidelines:

Two (2) of the following barrier methods in combination:

- Diaphragm with spermicide (cannot be used with cervical cap/spermicide)
- Cervical cap with spermicide (women who've never had a child)
- Contraceptive sponge (women who've never had a child)
- Male condom or female condom (cannot be used together)
- Hormonal contraceptive: oral contraceptive pill (estrogen/progestin pill or progestin-only pill), contraceptive skin patch, vaginal contraceptive ring, or subcutaneous contraceptive injection

OR

One (1) of the following:

- Intrauterine Device (IUD)
- Vasectomy of a female subject's male partner
- Contraceptive rod implanted into the skin

Privacy Risks

If your genetic research data are shared with unauthorized users, you may be at risk of loss of the privacy of your health data. This risk is minimized by protections described in the Confidentiality section below.

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WILL I BENEFIT FROM PARTICIPATING IN THIS STUDY?

If you agree to take part in this study, there may or may not be direct medical benefit to you. Information learned from this study may help other people in the future. The Sponsor will not provide you with ownership or any financial benefits that may result from this study.

WHAT OTHER CHOICES DO I HAVE IF I DO NOT TAKE PART IN THIS STUDY?

Instead of being in this study, you have other options including:

- Receiving treatment without participation on this study
- Treatment with other anti-cancer drugs
- No therapy with comfort care only

Please talk to your study doctor about these and other options along with their risks and benefits. Please ask any questions you may have and take as much time as you need to make your decision.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

You will not receive payment for taking part in this study. For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's web site at http://cancer.gov/clinicaltrials/understanding/insurance-coverage You can print a copy of the "Clinical Trials and Insurance Coverage" information from this web site. Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

Some of the tests or treatments used in this study may be part of standard care used to maintain your health and would be recommended even if you did not take part in this study. You or your insurance company will be responsible for the cost of this standard care. Pembrolizumab, tests, and procedures done for the sole purpose of the study, including tumor biopsies and blood drawn for research will be provided at no cost to you. If you have a biopsy as part of your standard care during any of the time-points when a research biopsy is required, the cost of the biopsy will be billed to you or your insurance. After tissue has been collected during a biopsy, a portion of the tissue will be used for the purposes of the study. If you do not require a biopsy as part of your standard care during the time-point when a research biopsy is required, you will have a biopsy for research purposes only, and the cost of the biopsy will not be billed to you or your insurance.

You may wish to discuss coverage with your insurance company before agreeing to participate in this research study.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?

If you become ill or are hurt while you are in the study, get the medical care that you need right away.

In the event that you are harmed as a result of your participation in this study, inform your study doctor immediately so you can access medical treatment.

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You and/or your health plan will be charged for this treatment in the usual manner. The study will not pay for standard medical treatment.

You still have the right to make a claim through the legal system even if you sign and date this form, accept medical care, or accept payment for medical expenses.

WHAT IF I WANT TO QUIT THE STUDY LATER ON?

Your participation in this study is completely voluntary. You should feel under no pressure to be in the study. If you decide not to be in the study, your decision to not participate will not in any way harm your relationship with your doctors or with Atrium Health. You are free to stop being in the study if you change your mind after entering it. This would not harm your relationship with your doctors or Atrium Health.

If you choose to withdraw from the study, please notify the study doctor in writing at:

Antoinette Tan, MD
[redacted]

The study doctor may choose to involuntarily withdraw you from the study for any reason.

We will tell you about new medical findings that may affect your willingness to continue in the study.

CONFIDENTIALITY

The records of this study will be kept private. In any sort of report we might publish, we will not include any information that will make it possible to identify a patient. Your record for this study may, however, be reviewed and/or photocopied by the sponsor, by Atrium Health, or by representatives of the Food and Drug Administration or other government agencies. To that extent, confidentiality is not absolute.

To ensure that your information collected for this study will be kept private, your name will not be used whenever possible. A code will be used instead of your name. All of your study data will be kept in a secure location.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans and most employers to discriminate against you based on your genetic information.

This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that the sponsor will get from this research.

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

All health insurance companies and group health plans and all employers with 15 or more people must follow this law.

AUTHORIZATION TO DISCLOSE HEALTH INFORMATION

If you wish to take part in this clinical study, you will be asked to sign this consent form. It allows the study sponsor and the study investigator to collect, process and pass on to the sponsor organizations any relevant personal health information collected from you during the study. These are activities routinely carried out during all clinical studies.

You have been told that personal information about you (including sensitive personal health information, such as your medical history and your racial/ethnic origin if relevant to the study) will be reviewed, collected on a computer database, stored in electronic or manual files, audited, and/or otherwise processed by:

- the study doctor and study staff,
- the study sponsor and/or its associated companies, Levine Cancer Institute,
- regulatory or other governmental authorities of the United States and other countries,
- other persons authorized by the study sponsor,
- Atrium Health employees,
- Caris Life Sciences employees (de-identified clinical data),
- Inivata Limited employees (de-identified clinical data)
- other persons or agencies as required by law or allowed by federal regulations.

You have been told that your personal data are being collected and processed to:

- check your suitability to take part in the study,
- monitor your treatment with the study drug,
- compare and pool study treatment results with those of other subjects in clinical studies,
- support the development of the study drug,
- support the licensing application for regulatory approval of the study drug in the world
- support the marketing, distribution, sale and use of the study drug anywhere in the world.

You have been told that your personal information may be processed within the U.S. or elsewhere in the world or transferred to or from the U.S. for review, processing and/or storage by an associated company or a carefully selected third-party organization. By signing this document, you explicitly consent to the transfer of your personal information, including sensitive personal information, collected during this clinical study, for review, processing and/or storage. Your personal health

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information may be further shared by the groups above. If shared by them, the information will no longer be covered by the Privacy Rule. However, the groups are committed to keeping your personal health confidential.

You may refuse this authorization to transfer your personal information. If you choose not to agree to this authorization, you might be ineligible to participate in the study. If you decide not to sign this authorization, that will not harm your relations with your doctors or with Atrium Health.

You have the right to inspect your medical record at any time. Your research record may be unavailable until the conclusion of the study. At that point, it will be available. Please speak with the study doctor if you desire to access your record.

You have been told whenever your personal information is processed; it will be kept confidential and secure, to the best of our ability. It will be used only for the purpose for which it was collected.

This Authorization does not have an expiration date. You have been told that according to the guidelines for good clinical practice, the study investigator and sponsor will keep your personal information for at least 6 years. If you do not withdraw this Authorization in writing, it will remain in effect indefinitely. If you wish to revoke authorization to use your personal information, you will notify the study doctor in writing at the address and telephone number listed on the first page of this form. Some of the data obtained from your record prior to your revocation may still be used if considered necessary for the study.

FINANCIAL DISCLOSURE

None of the doctors asking you to participate in this study has received or will receive money or other benefits for personal use from Merck Sharp & Dohme Corp, that developed pembrolizumab used in this study.

WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the Investigator at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, contact**:**

- By mail:

  Study Subject Adviser
  [redacted]

Affix Participant Barcode Label Here

- or call **toll free**: [redacted]
- or by **email**: [redacted]

Please reference the following number when contacting the Study Subject Adviser: Pro00019078.

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.

OPTIONAL TUMOR BIOPSIES

The study doctor and her associates (the investigators) are asking you to allow additional biopsies of your tumor to be collected at specific time points and used for the purposes of research. All information for the main study's informed consent form, still applies to this part of the informed consent.

Your study doctor would like to collect additional tumor biopsies within 5 days of Cycle 5 Day 1 and at the time of disease progression, if your disease progresses. Regardless of your decision to allow additional tumor biopsies to be taken, you may still participate in the main study, if you choose to. However, you must participate in the main study in order to be eligible for the additional biopsies.

The samples from your tumor biopsy will be stored at the Levine Cancer Institute Bio Specimen Repository, a place where human samples are securely stored and where any of your remaining archived and/or freshly collected samples will be stored.

If you decide, at a later date to withdraw your consent for any reason, you have the option not to allow Levine Cancer Institute to use your tumor samples for testing by contacting the study doctor at the telephone number or address listed on the first page of this form. At your request, tumor samples will be destroyed, only if they have not already been tested.

Do you give permission to have optional tumor biopsies for the purposes of research? Participation in these collections are optional, and refusing to participate will not affect your eligibility for the study or the study treatment given.

Yes_____ **No**_____ **Initials**_____

Affix Participant Barcode Label Here

OPTIONAL AND FUTURE STUDIES – BIO SPECIMEN COLLECTION

The study doctor and her associates (the investigators) are asking you to allow your blood to be collected and used for the purposes of research. In addition, the study doctor is also asking you to allow your tissue (including previously collected tissue and tissue collected as part of your participation in the study) to be stored for future, currently unplanned research after research testing on your tissue has been completed. All information for the main study's informed consent form, still applies to this part of the informed consent. Regardless of your decision to participate in this optional blood collection and/or tissue storage, you may still participate in the main study, if you choose to. However, you must participate in the main study in order to be eligible for participation in this optional blood collection and/or tissue storage.

If you agree to participate in the optional and future research - blood collection, we will ask to collect approximately 20 mL or about a tablespoon and a half of blood at each collection time point. We would like to collect blood before the first day of study treatment on this study, before cycle 3 day 1 of this study, before cycle 5 day 1 on this study, and after your study doctor has confirmed disease progression (if your disease progresses).

If you agree to participate in tissue banking for future research, we will store a portion of previously collected tissue and any tissue collected as part of your participation on this study to store for future, currently unplanned research.

If you agree to donate samples, they will be stored at the Levine Cancer Institute Bio Specimen Repository, a place where human samples are securely stored and where any of your remaining archived and/or freshly collected samples will be stored.

If you decide, at a later date to withdraw your consent for any reason, you have the option not to allow Levine Cancer Institute to use your blood samples and/or tissue for testing by contacting the study doctor at the telephone number or address listed on the first page of this form. Blood and tissue samples will be destroyed only if they have not already been tested.

Participation in these collections are optional, and refusing to participate will not affect your eligibility for the study or the study treatment given.

Do you give permission to have optional blood collections for the purposes of storage for future research?

Yes_____ **No**_____ **Initials**_____

Do you give permission to have a portion of your previously collected tissue and any tissue collected during the study to be stored for future research?

Yes_____ **No**_____ **Initials**_____

Affix Participant Barcode Label Here

TRIPLE NEGATIVE BREAST CANCER SUBJECTS ONLY: SUBJECT DERIVED XENOGRAFT

You are being asked to take part in this assessment, because you have different disease characteristics than some of the other subjects on this study, and have been diagnosed with triple negative breast cancer. Triple negative breast cancer means you do not express any of three common hormones (progesterone, estrogen) or protein (human epidermal growth factor receptor 2 – Her2/neu) receptors in your breast cancer. These receptors are proteins that detect specific hormones to signal cellular growth. By choosing to participate on this study, you are agreeing to allow part of your pre-study treatment tumor sample and blood to be used for the purposes of research. All of the above information, for the main part of the study, still applies to this part of the informed consent.

If you have triple negative breast cancer, and you still have enough remaining tumor sample after testing your tumor for cellular characteristics and biomarker expression, we will take a portion of the collected pre-study treatment tumor specimen and a blood sample and send it to an external laboratory, Champions Oncology Inc. laboratory. Your name and other personal identifying information will not be provided to this external lab, and your specimens will be labeled with a unique identifier code that is assigned to you. De-identified clinical information will be provided to Champions.

A part of your tumor will be injected and regrown in mice that are immune deficient. Immune deficient means that the immune system isn't strong enough to fight disease or is absent. Your blood sample will be used to compare to the regrown tumor sample. Through this process, a model of your disease can be maintained and tested for translational or laboratory purposes. The goal is to evaluate tumor response and resistance to treatment, and to sequence (determine the order of) the tumor DNA structure and the regular DNA blood sample for comparison.

If you decide, at a later date to withdraw your consent for any reason, you have the option not to allow Levine Cancer Institute to use your tumor sample for testing by contacting the study doctor at the telephone number or address listed on the first page of this form. Tumor and/or tissue samples will be destroyed, only if they have not already been tested.

Participation in this study is optional, and refusing to participate will not affect your relationship with your doctors, Levine Cancer Institute, or Atrium Health.

If you have any additional questions, you can ask your study doctor for more explanation.

Do you give permission to use your tumor sample for the purposes of research?

Yes_____ **No**_____ **Initials**_____

Affix Participant Barcode Label Here

STATEMENT OF CONSENT

I have read this form and its contents were explained to me. I agree to be in this research study for the purposes listed above. All of my questions were answered to my satisfaction. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing and dating this form. Dr. Tan, one of her associates, or her designee, will give me a copy of this signed and dated form.

_____ ____/____/____ _____
Signature of Research Subject Date Time

_____
Printed Name of Research Subject

STATEMENT OF PERSON EXPLAINING CONSENT

I have carefully explained to the subject the nature and purpose of the above study. There has been an opportunity for the subject to ask questions about this research study. I have been available to answer any questions that the subject has about this study.

_____ ____/____/____ _____
Signature of Person Explaining Consent Date Time

_____
Printed Name of Person Explaining Consent

Affix Participant Barcode Label Here