Research Consent Form
Dana-Farber/ Harvard Cancer Center
BIDMC/BCH/BWH/DFCI/MGH/Partners Network Affiliates

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Protocol Title:

ADVANCE (A Pilot Trial) ADjuVANt Chemotherapy in the Elderly: Developing and Evaluating Lower-Toxicity Chemotherapy Options for Older Patients with Breast Cancer

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Main Consent

INTRODUCTION AND KEY INFORMATION

All research is voluntary. It is your choice whether you take part in this research or not.

The following is a short summary of this research study to help you decide whether you would like to be a part of this study. More detailed information is provided later in this form.

For purposes of this research, you will be referred to as a "participant."

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

You are invited to take part in in this research study, because you have breast cancer, are at least age 70, and have been recommended to receive chemotherapy by your treatment team.

2. Why is this research being done?

This clinical trial is dedicated to patients age 70 and older and is focused on understanding how we can improve upon breast cancer outcomes for older women. A main focus of this study is to carefully study how chemotherapy is tolerated in this group of patients.

3. What does this research study involve and how long will it last?

This research study involves chemotherapy medications which are commercially available and not invesitgational.

The names of the study drugs involved in this study are based on your tumor subtype and include:

- **Paclitaxel and carboplatin** if your cancer subtype is triple negative, meaning it does not have the three receptors that are typically tested in breast cancer (estrogen receptor [ER], progesterone receptor [PR], and human epidermal growth factor receptor 2 [HER2])
- **Paclitaxel and cyclophosphamide** if your cancer subtype is ER or PR positive, meaning it is hormone receptor-positive and HER2-negative

The research study procedures include: screening for eligibility and study treatment including evaluations, surveys, and follow up visits.

Regardless of your chemotherapy group, you will receive study treatment for 12 weeks and will be followed for up to 2 years after treatment is complete.

It is expected that about 40 people will take part in this research study.

Information about you and your health is personal and private. Generally, it cannot be obtained without your written permission. By signing this form, you are providing that permission and your information may be obtained and used in accordance with this informed consent and as required or allowed by law. This means that researchers may obtain information regarding your past medical history, as well as specimens and samples from previous health care providers such as hospitals and labs.

4. What are the risks to participating in this study?

We hope you will tolerate your treatments very well while on this study. However, there are risks to taking part in any research study. In this study, the potential risks are mostly related to the potential side effects of chemotherapy. Although each agent has its own set of potential side effects which are discussed in more detail later in this document, in general, patients receiving chemotherapy such as those administered in this study include:

- Low blood counts
- Fatigue
- Hair loss
- Numbnsss of pain and hands of feet (neuropathy)
- Abnormal liver function

- Flushing or allergic reaction to the chemotherapy agents

5. Will being in this study benefit me in any way?

We do not know if taking part in this study will benefit you but your treatment team has recommended chemotherapy because they think it will lower your risk for recurrence of your cancer. This study may help researchers learn information that could help people in the future.

6. What are my options?

If you decide to participate, please sign and date at the end of this form.

We will give you a copy and you can refer to this consent form at any time during the research study.

If you choose not to participate in this research study, you will discuss other treatment options with your treatment team.

A. WHY IS THIS RESEARCH STUDY BEING DONE?

This clinical trial is dedicated to patients age 70 and older and is focused on understanding how we can improve upon breast cancer outcomes for older women, a group of patients who often do worse than younger patients and who are not well represented in clinical trials to date. Through this clinical trial, we aim to better understand the side effects, experiences, and changes in physical function that may occur with chemotherapy. We are also very interested in the genomics (or gene-changes) and biological changes that may occur in breast cancers in older women that may be different from the changes we see in younger patients.

Even though the chemotherapy agents being used in this study are used frequently when treating breast cancer, we have limited information on how these agents are tolerated in older patients. This research study is called a Feasibility Study, because we will be closely monitoring how easily it is to administer chemotherapy to a relatively small group of participants (up to 40) and to what degree side effects occur. We will administer commercially available chemotherapy agents used in breast cancer in the *specific* setting of the treating older patients with early-stage breast cancer and with some mild modification of how these agents are given and in what combination.

For participants with triple negative breast cancer, **paclitaxel and carboplatin** will be administered in standard, weekly doses. Both agents are FDA-approved for use in early breast cancer. However, carboplatin and paclitaxel are not typically used as a 'stand-alone' treatment for breast cancer, meaning they are often used together along with other chemotherapy agent(s) over a longer period. This clinical trial does not limit the use of other chemotherapy or other treatments being recommended for your cancer, but any other recommended treatments would be given after you receive your paclitaxel and carboplatin on the clinical trial.

For participants with hormone receptor-positive breast cancer, **paclitaxel and cyclophosphamide** will be administered, which are both FDA-approved agents to treat breast cancer as part of a longer regimen to treat early breast cancer. In this clinical trial we are modifying the way the chemotherapy is delivered so that it may be more tolerable than the longer treatment course. This clinical trial does not limit the use of other chemotherapy or other treatments being recommended for your cancer, but any other recommended treatments would be given after you receive your paclitaxel and carboplatin on the clinical trial.

In this research study, we are...

- Examining how tolerable the chemotherapy treatments are for you and what side effects you experience
- Examining whether doses have to be skipped or lowered because of a side effect
- Examining what happens to your physical function over time
- Examining what happens to you and your health over time
- Exploring gene changes in your blood and tumor and how it may help understand what happens to your health

B. WHAT OTHER OPTIONS ARE THERE?

Taking part in this research study is voluntary. Instead of being in this research study, you have other options which may include the following

- Receive standard treatment including standard chemotherapy
- Take part in another research study.
- Receive the same drugs, but not as part of a research study.
- Receive no chemotherapy specific to your cancer.

Please talk to the research doctor about your options before you decide whether you will take part in this research study.

C. WHAT IS INVOLVED IN THE RESEARCH STUDY?

You will be assigned to receive 12 weeks of carboplatin-paclitaxel (cohort1) or 12 weeks of cyclophosphamide-paclitaxel (cohort 2) based on your tumor subtype. There is no 'placebo' or randomization as part of this study. Everyone on this clinical trial has been recommended to receive chemotherapy by their treating provider.

Cohort 1: carboplatin and paclitaxel (if your cancer is triple negative)
Cohort 2: cyclophosphamide and paclitaxel (if your cancer is hormone receptor-positive)

Sometimes it is hard to keep track of all of the details and procedures that are part of a research study. We will describe them in this consent form and you can refer to this at any time during the research study.

Before the research starts (screening):
After signing this consent form, you will be asked to undergo some screening tests or procedures to find out if you can be in the research study. Many of these tests and procedures are likely to be part of regular cancer care and may be

done even if it turns out that you do not take part in the research study. If you have had some of these tests or procedures recently, they may or may not have to be repeated.

- **A medical history,** which includes questions about your health, your age, current medications, and any allergies.

- **A willingness to complete surveys before treatment, the start of every treatment cycle (every 21 days), at the end of treatment, and approximately 3 months after chemotherapy ends** that focus on how you are feeling, what side effects you are having, and your overall health, physical function, and social support.

If these tests show that you are eligible to participate in the research study, you may begin the study treatment. If you do not meet the eligibility criteria, you will not be able to participate in this research study.

Additional research procedures to be performed at the time of screening but not required to determine eligibility:

- **Previously collected tumor sample.** With this consent, we will request that a small sample of your breast tissue from your biopsy or surgery be sent to a centralized laboratory and stored for future research. There is very little known about the genetic changes in breast cancers for patients 70 and older and this part of the study will provide important information. You do not need to undergo any additional biopsies or surgeries to obtain this tissue. It will be sent from your biopsy or your breast surgery.

- **Permission to collect a fresh tissue sample, only if you are a participant at Dana-Farber and have not already had surgery and your chemotherapy is being administered before you have surgery.** We will ask permission to take a small part of this surgical sample to look for the tumor's environment in your tissue and genomic studies or DNA studies to look at possible DNA changes that may have occurred in your cancer.

- **Research blood tests.** An extra 1-2 tablespoons of blood will be collected for research at the same time you have blood work for your chemotherapy.

- **Surveys (Patient Reported Outcomes and Questionnaire):** You will be asked to fill out surveys that will take you approximately 30 minutes to complete. These surveys will ask you questions about any symptoms you are feeling before you start chemotherapy, your physical function, social support, medications, medical problems, and mood. If you have a hard

time completing any of the questions or tasks, a member of the research team will help you.

- **A brief test of your memory** which will include a series of questions (note: your provider may be notified if significant problems are found with your memory).

- **'Up and go' test**: A member of the study team will time you as you get up from a chair, walk 10 feet, and return to the chair.

Study Treatment Overview:

- **Cohort 1: Infused Study Drug(s):** You will be given both study treatments carboplatin and paclitaxel once every 7 days into your vein (by intravenous infusion). Each cycle occurs when three weeks of treatment have passed. Treatment will continue for 12 weeks (or 4 cycles). If you miss a treatment, your provider may add it to the end and it could go longer than 12 weeks.

- **Cohort 2: Infused Study Drug(s):** You will be given paclitaxel once every 7 days and the cyclophosphamide every three weeks into your vein (by intravenous infusion). This will continue for 12 weeks (4 cycles, each cycle being three weeks long). If you miss a treatment, your provider may add it to the end and it could go longer than 12 weeks.

- **Pre-medications:** You may be pre-medicated with drugs to reduce the chance of having a sensitivity reaction to the study treatment. If you tolerate the study treatment without a reaction, then pre-medications may be changed by your doctor. You will also be given medications to help prevent nausea that may occur with treatment.

If you are in cohort 1 or 2, you will be seen every week for treatment in the infusion center and will see your treatment team (MD/NP/PA) at the start of each cycle, every three weeks. If you need to be seen more often because of side effects, your providers can change this schedule as needed.

Every three weeks while on treatment:

- **Clinical Exams:** On the first day of each treatment cycle, every 21 days, we will have you see your provider for an evaluation and symptom review. During this visit you will have a physical exam and you will be asked questions about your general health and specific questions about any problems that you might be having and any medications you may be taking.

- **Patient-reported outcomes**: We will ask you to fill out a survey about any symptoms you are having on treatment.

- **Medical record review:** We will look at your medical records periodically to see how you are doing, whether you have been hospitalized, and to understand your treatment patterns, doses skipped or lowered. We may also reach out to you by phone or email if we cannot find your health status from your medical records.

Cycle 3 Day 1 Visit

- **Clinical Exam**
- **Patient-reported outcomes**
- **Medical Record Review**

- **Survey (Questionnaire):** You will be asked to fill out a survey that will again you questions about your physical function, social support, medications, medical problems, and mood. If you have a hard time completing any of the questions or tasks, a member of the research team will help you.

- **A brief test of your memory** (note: your provider may be notified if significant problems are found with your memory).

- **'Up and go' test**: A member of the study team will time you as you get up from a chair, walk 10 feet, and return to the chair.

- **Research blood tests**: We will take approximately 1-2 tablespoons of blood, at the same time as your clinical blood tests ordered before your chemotherapy, for research.

End of Chemotherapy

- **Patient-reported outcomes**: We will ask you to fill out a survey about any symptoms you are having on treatment.

- **Survey (Questionnaire):** You will be asked to fill out a survey that will again you questions about your physical function, social support, medications, medical problems, and mood. If you have a hard time completing any of the questions or tasks, a member of the research team will help you.

- **A brief test of your memory** (note: your provider may be notified if significant problems are found with your memory).

- **'Up and go' test**: A member of the study team will time you as you get up from a chair, walk 10 feet, and return to the chair.

- **Research blood tests**: At the start of cycle 3 and at the end of chemotherapy, we will take approximately 1-2 tablespoons of blood, at the same time as your clinical blood tests ordered before your chemotherapy, for research.

Three months after chemotherapy completes:
We would like to see how you are recovering from your chemotherapy treatments and ask for the following:

- **Patient-reported outcomes**: We will ask you to fill out a survey about any symptoms you are having on treatment.

- **Survey (Questionnaire):** You will be asked to fill out a survey that will again you questions about your physical function, social support, medications, medical problems, and mood. If you have a hard time completing any of the questions or tasks, a member of the research team will help you.

- **Medical record review:** We will look at your medical records periodically to see how you are doing, whether you have been hospitalized, and to understand your treatment patterns, doses skipped or lowered. We may also reach out to you by phone or email if we cannot find your health status from your medical records.

- **A brief test of your memory** (note: your provider may be notified if significant problems are found with your memory).

- **'Up and go' test**: A member of the study team will time you as you get up from a chair, walk 10 feet, and return to the chair.

Twelve months after chemotherapy completes:
We would like to see how you are recovering from your chemotherapy treatments and ask for the following:

- **Clinical Exam:** During this visit you will have a physical exam and you will be asked questions about your general health and specific questions about any problems that you might be having and any medications you may be taking.

- **Patient-reported outcomes**: We will ask you to fill out a survey about any symptoms you are having on treatment.

- **Survey (Questionnaire):** You will be asked to fill out a survey that will again you questions about your physical function, social support, medications, medical problems, and mood. If you have a hard time completing any of the questions or tasks, a member of the research team will help you.

- **Medical record review:** We will look at your medical records periodically to see how you are doing, whether you have been hospitalized, and to understand your treatment patterns, doses skipped or lowered. We may also reach out to you by phone or email if we cannot find your health status from your medical records.

- **A brief test of your memory** (note: your provider may be notified if significant problems are found with your memory).

- **'Up and go' test**: A member of the study team will time you as you get up from a chair, walk 10 feet, and return to the chair.

Research Study Plan:

	Screening	Day 1 of each cycle (every 3 weeks)	Cycle 3, day 1	End of treatment (approx.12 weeks)	3 months after chemotherapy ends	12 months after chemotherapy ends	For up to 2 years after treatment complete
Receive Chemotherapy		Weekly for 12 weeks					
Medical Record review & Physical Exam	X	X	X	X	X	X	
Survey (Questionnaire), "Up and Go" Test, Brief Memory Test	X		X	X	X	X	
Patient reported symptoms	X	X		X	X	X	
Research Blood Test*	X		X	X			
Tumor sample collected on previously collected tissue	X						
Fresh (new) tissue for those receiving pre-operative chemotherapy only				X (DFCI participants only at time of surgery)			
Medical record review or phone call to see how you are doing							X

*Note: you will also have blood checked prior to each chemotherapy treatment which is considered routine care and not mandatory for the study

Up to 2 years after chemotherapy completion:

Once treatment ends on this clinical trial, you may be recommended for additional treatment with surgery, radiation, additional chemotherapy, or hormonal therapy, depending on your cancer's characteristics. Over time, we would like to keep track of your medical condition. We would like to do this by calling you on the telephone about every 6 months to see how you are doing, calling your designated person, or by looking at your medical record. Keeping in touch with you and checking your condition every year helps us look at your long-term outcomes.

In addition, you can stop participating in the research study at any time, however, the FDA requires that any information collected up to the point of your withdrawal cannot be removed from the study.

Additional information about specimens and data collected as part of this study:

- **Biobanking:** Biological specimens (such as blood, tissue, or saliva) will be collected and shared with an outside lab or collaborator for analysis. The specimens will not be identifiable. The specimens will be banked for future use.
- **Data Collection:** Data will be collected and shared with an outside collaborator for analysis. The data will not be identifiable. The data will be banked for future use.

D. WHAT ARE THE RISKS OR DISCOMFORTS OF THE RESEARCH STUDY?

There are risks to taking part in any research study. One risk is that you may get a study drug that does not help treat your disease or that makes your condition or disease worse. Another risk is that there may be side effects.

All cancer treatments can have side effects, which can range from mild and reversible to severe, long lasting and possibly life-threatening. There is a great deal of variability among side effects of different cancer treatments and between individuals. In a research study, all of the risks or side effects may not be known before you start the study. **You need to tell your doctor or a member of the study team immediately if you experience any side effects.**
Everyone in the research study will be watched carefully for side effects. You will be monitored during the administration of study drugs to keep track of your blood counts and organ function, particularly your kidney and liver function. If you experience side effects, they may go away after you stop taking the study drug. Some side effects can be mild; but others can be long lasting and may never go away. Some may be life-threatening or fatal.

Since the effect of the study drug(s) taken with other medications may not be known, it is important that you tell the research doctor about all prescription and non-prescription drugs, herbal preparations and nutritional supplements that you are taking or planning to take. There may also be some foods that you should avoid while on this research study and your research doctor will review this information with you.

During the research study, you will be notified of newly discovered side effects or significant findings, which may affect your health or willingness to participate. You may be asked to sign a new consent form that shows that you have been informed of new information relating to this research study.

Risks Associated with Paclitaxel (Cohort 1 and 2):

Likely (More than a 50% chance that this will happen)

- Low red blood cell count (anemia), which can cause tiredness and shortness of breath. This may require a blood transfusion if severe, though most anemias do not require this
- Low white blood cell count which may put you at increased risk for infection
- Low numbers of platelets, which may cause bleeding and bruising
- Hair loss
- Mild numbness and pain of the hands and feet ('neuropathy') that sometimes worsens with additional study treatment and may not disappear after the drug is stopped
- Nausea or vomiting

Frequent (Between a 11-50% chance that this will happen)

- Infection
- Fever and low white blood cell count
- Slowing of heart rate which can be serious
- Irregular heartbeats
- Mild allergic reaction
- Muscle weakness of the whole body
- Muscle and joint aches
- Diarrhea
- Sores in the mouth or esophagus, also called mucositis
- Fatigue
- Lightheadedness
- Headaches
- A sensation of flashing lights or spots
- Abnormal kidney tests, which indicate that the kidneys may not be working properly
- An increase in triglycerides or blood lipid levels
- Abnormal liver function tests
- Confusion, mood changes
- Skin irritation and swelling if the drug leaks from the vein into which it is being injected into the surrounding skin

Occasional (Between a 1-10% chance that this will happen)

- Severe numbness and pain of the hands and feet ('neuropathy') that sometimes worsens with additional study treatment and may not disappear after the drug is stopped

- Severe allergic reaction which can be serious or life threatening
- Severe muscle and joint pains

Rare (Less than a 1% chance that this will happen)
- Liver damage or failure

Risks Associated with Cyclophosphamide (Cohort 2):

Frequent (Between a 11-50% chance that this will happen)
- Hair loss
- Nausea/vomiting
- Appetite change
- Diarrhea
- Stomach cramps, pain in abdomen due to cramping
- Mouth sores
- Inflammation of your bladder with severe bleeding; blood in urine
- Low platelet count, which can decrease the clotting of your blood and increase your risk for bleeding and bruising
- Low red blood cell count (anemia), which can cause tiredness and shortness of breath. This may require a blood transfusion if severe, though most anemias do not require this
- Low white blood cells, which may increase the risk for infection

Occasional (Between a 1-10% chance that this will happen*)*
- Facial flushing
- Headache
- Skin rash
- Changes in electrolytes (body salts) which usually do not cause any symptoms but can sometimes cause fatigue, muscle weakness, cramping, rigidity, irregular heartbeat or seizures. Rarely, this can be life threatening and could require hospitalization and intravenous treatment.
- A blood clot. This most commonly forms in the legs but can develop anywhere in the body. A piece of clot may travel to the lung and cause sudden blockage in a lung blood vessel. This is known as a pulmonary embolism and is a serious condition that can cause permanent damage to part of your lung from lack of blood flow to your lung tissue; low oxygen levels in your blood; damage to other organs in your body from not getting enough oxygen; if a clot is large, or if there are many clots, a pulmonary embolism can cause death
- Nasal congestion
- Sneezing during and after the infusion

Rare (Less than a 1% chance that this will happen)

- Liver damage or failure
- Seizures

Rare, but serious (Less than a 1% chance that this will happen)

- Heart damage where the muscle becomes damaged and the heart doesn't pump properly which can cause weakness and tiredness, fluid retention, and fluid build-up in the lungs, which can cause shortness of breath. This may be serious or life-threatening.
- Inflammation of the lungs, which can cause shortness of breath and difficulty breathing. If severe, this can be life-threatening
- Allergic reaction that may include a rash, hives, fever, difficulty breathing, and low blood pressure. Although almost always reversible with treatment, it can be severe or life threatening

Other adverse reactions that have been rarely reported include:

- Bleeding of the colon
- Abnormally high levels of enzymes produced by the liver, meaning that your liver is not functioning properly and can cause fatigue and jaundice (yellowing of the skin and eyes). Although this is usually mild and reversible, this can be serious or life threatening.
- Elevated uric acid levels, which may worsen kidney function; cause joint pain (gout) and kidney stones. May cause kidney failure, which may be reversible
- Low potassium, which can cause an abnormal heart rate. This could cause an irregular heartbeat, which can be serious and life threatening
- General feeling of discomfort (malaise)
- Skin reaction that develops when chemotherapy is administered during or after radiation treatment, characterized by one or more of symptoms of redness, tenderness, swelling, peeling, pain and discoloration that can be severe or disfiguring.
- Kidney dysfunction: when the kidneys do not work properly, wastes can build up in your blood, leading to swelling in the arms and legs, tiredness and weakness. This could become severe, requiring hospitalization and dialysis to clean the wastes out of your blood. If the wastes are not removed from your blood, this could cause seizures and be life-threatening. Your kidney function will be monitored closely through blood and urine tests. Any kidney damage that could occur is usually reversible
- Cancer of the bladder
- Stevens-Johnson syndrome: A skin condition that causes painful

blisters and sores of the skin and mucous membranes, especially in the mouth. May cause difficulty eating and swallowing. This is similar to the skin damage from a severe burn and is serious and life-threatening.
- Toxic epidermal necrolysis: Severe skin and gut lining reaction that may include rash and sloughing or dead tissue. This may manifest as various blisters, hives and other lesions in various locations in the body including palms and soles, face and other extremities. This is serious and may be life-threatening.
- Weakness

Risks Associated with Carboplatin (Cohort 1):

Likely (More than a 50% chance that this will happen)
- Nausea
- Vomiting
- Low platelet counts (thrombocytopenia). This may increase your risk for skin bruising, nose bleeds, and bleeding from the gums.
- Low red blood cell counts (anemia). This may make you feel weak and tired.
- Low white blood cell counts (leukopenia and neutropenia). These put you at higher risk for infection

Frequent (Between a 11-50% chance that this will happen):
- Low sodium level in the blood
- Low potassium level in the blood
- Low calcium level in the blood
- Low magnesium level in the blood
- Increased liver enzymes in the blood
- Pain
- Unusual tiredness or weakness

Occasional (Between a 1-10% chance that this will happen*)*
- Diarrhea
- Constipation
- Sores, ulcers, or white patches in the mouth and throat
- Pain, burning, or tingling in the hands or feet
- Pain, itching, redness, swelling, blisters, or sores in the place where the medication was injected
- Loss in ability to taste food
- Pale skin
- Hair loss
- Fainting
- Dizziness

- Sudden changes in vision, including color vision
- Abnormal kidney function tests
- Swelling of the face, arms, hands, feet, ankles, or lower legs
- Shortness of breath with everyday activity or when lying flat
- Ringing in ears and difficulty hearing
- Allergic reaction (rash, itching, skin redness and swelling, shortness of breath, and low blood pressure)

Risks of Biobanking:
Generally, hospitals will keep some of your tissue. This tissue may be used to help treat your cancer in the future. There is a small risk that when this tissue sample is submitted to the biobank for this optional sample collection, your tissue could be used up.

Non-Physical Risks:
Because of side effects or the time required for tests and clinic visits while you are on this research study, you may be unable to keep up with your normal daily activities.

The questionnaires used in this study may be upsetting. If you find the questionnaires upsetting, you may speak with the research doctor or ask to be referred for additional emotional support.

E. WHAT WILL HAPPEN IF I AM REMOVED FROM THE STUDY OR DECIDE TO END MY PARTICIPATION IN THE RESEARCH?

You may be taken off the research study for many reasons including if:

- It is considered to be in your best interest
- The study treatment or procedures are found to be unsafe or ineffective
- There is any problem with following study treatments and procedures
- Your condition worsens
- A decision is made to close the study
- Or for other unforeseen reasons that make it necessary to stop your participation in the research study

You can also choose to stop participating in the research study at any time. Tell the research doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop. Leaving the research study will not affect your medical care outside of the research study.

It is important to tell the research doctor if you are thinking about stopping so your research doctor can evaluate the risks from stopping the paclitaxel, cyclophosphamide, or carboplatin.

In some cases, the abrupt stopping of a drug can have risks in itself. Another reason to tell your research doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

It is important to note that although you may withdraw from study participation, the FDA requires that any information collected up to the point of your withdrawal cannot be removed from study records.

If you decide to withdraw from a study that involves de-identified samples and data, it will not be possible to remove the samples and data that have already been submitted to a database or biobank.

F. WILL I BE PAID TO TAKE PART IN THIS RESEARCH STUDY?

You will not be paid for participating in this study.

We may use your samples and information to develop a new product or medical test to be sold. The sponsor and hospital may benefit if this happens. There are no plans to pay you if your samples are used for this purpose.

G. WHO IS SUPPORTING THIS RESEARCH?

The sponsor of this study is Dana Farber/Partners Cancer Care on behalf of Dana Farber/Harvard Cancer Center. The Alliance for Clinical Trials in Oncology NCORP (National Cancer Institute Community Oncology Research Program) Research Base Cancer Control Program is supporting this research study by providing funding to support the clinical trial. The actual chemotherapy agents in this study will be provided by commercial insurance.

H. WHAT ARE YOUR COSTS?

Taking part in this research study may lead to added costs to you or your insurance company.

You or your insurance company will be charged for portions of your care during this research study that are considered standard care. Standard of care is the care that you would receive regardless of whether you were enrolled in the study or not. You may be responsible for co-payments, co-insurance, premiums and deductibles that are typical for your insurance coverage. This includes the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests, done for research only, are supplied at no charge.

All of the chemotherapy on this study is commercially available which means that the FDA has approved it for use in patients with another type of cancer. Because there is evidence that supports using this drug in patients with your type of cancer, you or your insurance company will be billed for the cost of each chemotherapy agent.

If you have questions about your insurance coverage, or the items you might be required to pay for, please call financial services for information. The contact information for financial services are:

- **Dana-Farber Cancer Institute**: (617) 632-3455
- **Dana-Farber/Brigham and Women's Hospital in Clinical Affiliation with South Shore Hospital**: (781) 624-4329
- **Dana-Farber at Milford Regional Cancer Center (MRCC):** 508-488-3700
- **Dana-Farber at St. Elizabeth's Medical Center (SEMC): (**617) 632-4595

The National Cancer Institute provides an online resource to help people participating in cancer clinical trials understand which services their insurance company is required by law to pay. This can be found at the website below or can be provided by the study team:

www.cancer.gov
or 1-800-4-CANCER (1-800-422-6237)

I. WHAT HAPPENS IF I AM INJURED OR BECOME SICK BECAUSE I TOOK PART IN THIS RESEARCH STUDY?

If you think you have been injured as a result of taking part in this research study, tell the person in charge of this research study as soon as possible. The research doctor's name and phone number are listed in this consent form.

The treating hospital will offer you the care needed to treat injuries directly resulting from taking part in this research. These treatments may be billed to you or your insurance company. You will be responsible for deductibles, co-payments and co-insurance. There are no plans for the sponsor of this study, Dana Farber/Partners Cancer Care on behalf of Dana Farer/Harvard Cancer Center, to pay you or give you other compensation for the injury.
You do not give up your legal rights by signing this form.

We will need to collect certain personal information about you for insurance or payment reporting purposes, such as your name, date of birth, gender, social security number or Medicare identification number and information related to this research study. We may be required to report this information to the Centers for Medicare & Medicaid Services. We will not use this information for any other purpose.

If you go to the Emergency Room or to another hospital or doctor it is important that you tell them that you are in this research. If possible, you should give them a copy of this consent form.

J. WHOM DO I CONTACT IF I HAVE QUESTIONS ABOUT THE RESEARCH STUDY?

If you have questions about the study, please contact the research doctor or study staff as listed below:

Dana-Farber Cancer Institute
- Rachel Freedman, MD, MPH: (617) 632-3800

Dana-Farber/Brigham and Women's Cancer Center in Clinical Affiliation with South Shore Hospital (DFCI @ SSH)
- Meredith Faggen, MD: 781-624-4800

Dana-Farber at Milford Regional Cancer Center (MRCC):
- Michael Constantine, MD at (508) 488-3700

Dana-Farber at St. Elizabeth's Medical Center (SEMC):
- Caroline Block, MD at (617) 632-4595

24-hour contact numbers:
DFCI: Dr. Rachel Freedman at (617) 632-3352.
DFCI @ SSH: Meredith Faggen, MD at (781) 624-4800
DFCI @ MRCC: Michael Constantine, MD at (508) 488-3700
DFCI @ SEMC: Caroline Block, MD at (617) 632-4595

For questions about your rights as a research participant, please contact a representative of the Office for Human Research Studies at Dana-Farber Cancer Institute (617) 632-3029. This can include questions about your participation in the study, concerns about the study, a research related injury, or if you feel/felt under pressure to enroll in this research study or to continue to participate in this research study.

K. RETURN OF RESEARCH RESULTS

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 may contact you to let you know what they have found. However, because these tests are not being done in 'real-time', are providing initial and exploratory information and do not have clear actions that should come from the results, you will not hear about the results from these tests during your involvemen the study.

L. CLINICALTRIALS.GOV (CT.GOV)

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.

M. FUTURE USE OF DATA AND SPECIMENS

Your personal information and/or biospecimens collected during this study may be stored and used for future research. Any personal identifiers will be removed so that the information or samples cannot be linked back to you. As a result, we will no longer be able to identify and destroy them.

Investigators, including investigators from collaborating institutions, can request this data and samples for new research. Samples and data may also be shared with outside non-profit academic investigators as well as with for-profit pharmaceutical investigators or commercial entities, with whom we collaborate.

You will not be asked to provide additional informed consent for the use of your de-identified information or samples in future research.

Future research studies may include genetic research. Your genes are unique to you. At this time, you cannot be identified through this research. There is a risk that you might be reidentified in the future as genetic research progresses

N. CONFIDENTIALITY

We will take measures to protect the privacy and security of all your personal information, but we cannot guarantee complete confidentiality of study data.

Medical information created by this research study may become part of your hospital medical record and may be forwarded to your primary doctor. Information that does not become part of your medical record will be stored in your study file. It may also become part of a DF/HCC research database called CORIS.

Participation in this study involves providing a specimen of your tissue; please know that if the research doctor leaves the institution, the research and the tissue might remain at the DF/HCC or might be transferred to another institution.

The study team plans to publish the results of this research study and when we do, we may be asked to make the data we collect available to other researchers. We will not include information that identifies you in any publications or to the researchers who request the data to do additional research.

Your de-identified specimens or genetic data may also be placed into one or more publicly-accessible scientific databases. Through such databases, researchers from around the world will have access to de-identified samples or data for future research.

There is a risk that deidentified research data that is shared with outside collaborators may be reidentified. When deidentified data and specimens are shared with outside collaborators agreements limit what the outside collaborators can do with the information to help prevent reidentification.

O. GENETIC RESEARCH

This research will involve genomic testing.

The Genetic Information Nondiscrimination Act of 2008 (GINA) is a federal law that protects Americans from being treated unfairly because of differences in their DNA that may affect their health, and may prevent discrimination by health insurers and employers based on genetic information. GINA is intended to ease concerns about discrimination that might keep some people from getting genetic tests that could benefit their health, and enable people to take part in research studies such as this without fear that their DNA information might be used against them by health insurers or their workplace. This protection does not extend to disability or life insurance. Additional information can be found at http://www.genome.gov/10002328.

As part of this study, your de-identified specimens or genetic data may be placed into one or more publicly-accessible scientific databases, such as the National Institutes of Health's Database for Genotypes and Phenotypes (dbGaP). Through

such databases, researchers from around the world will have access to de-identified samples or data for future research.

P. PRIVACY OF PROTECTED HEALTH INFORMATION (HIPAA AUTHORIZATION)

The Health Insurance Portability and Accountability Act (HIPAA) is a federal law that requires Dana-Farber/Harvard Cancer Center (DF/HCC) and its affiliated research doctors, health care providers, and physician network to protect the privacy of information that identifies you and relates to your past, present, and future physical and mental health conditions ("protected health information"). If you enroll in this research study, your "protected health information" will be used and shared with others as explained below.

1. What protected health information about me will be used or shared with others during this research?

- Existing medical records, including mental health records.
- New health information created from study-related tests, procedures, visits, and/or questionnaires

2. Why will protected information about me be used or shared with others?

The main reasons include the following:

- To conduct and oversee the research described earlier in this form;
- To ensure the research meets legal, institutional, and accreditation requirements;
- To conduct public health activities (including reporting of adverse events or situations where you or others may be at risk of harm); and
- To provide the study sponsor with information arising from an adverse event or other event that relates to the safety or toxicity of the drug(s) used in the study and for the purpose of this or other research relating the study drug(s) and their use in cancer;
- To better understand the diseases being studied and to improve the design of future studies; and,
- Other reasons may include for treatment, payment, or health care operations. For example, some medical information produced by this research study may become part of your hospital medical record because the information may be necessary for your medical care. (You will also be given a notice for use and sharing of protected health information.)

3. Who will use or share protected health information about me?

- DF/HCC and its affiliated research doctors and entities participating in the research will use and share your protected health information. In addition, other DF/HCC offices that deal with research oversight, billing or quality assurance will be able to use and share your protected health information.

4. With whom outside of DF/HCC may my protected health information be shared?

While all reasonable efforts will be made to protect the confidentiality of your protected health information, it may also be shared with the following entities:

- Outside individuals or entities that have a need to access this information to perform functions relating to the conduct of this research such as analysis by outside laboratories on behalf of DF/HCC and its affiliates (for example, data storage companies, insurers, or legal advisors), including but not limited to:
    - The Broad Institute of MIT
    - Research Laboratories/Collaborators affiliated with Brigham and Women's Hospital
- The sponsor(s) of the study, its subcontractors, representatives, business partners, and its agent(s)
- Other research doctors and medical centers participating in this research, if applicable
- Federal and state agencies (for example, the Department of Health and Human Services, the Food and Drug Administration, the National Institutes of Health, and/or the Office for Human Research Protections), or other domestic or foreign government bodies if required by law and/or necessary for oversight purposes. A qualified representative of the FDA and the National Cancer Institute may review your medical records.
- Hospital accrediting agencies
- A data safety monitoring board organized to oversee this research, if applicable

Some who may receive your protected health information may not have to satisfy the privacy rules and requirements. They, in fact, may share your information with others without your permission.

5. For how long will protected health information about me be used or shared with others?

- There is no scheduled date at which your protected health information that is being used or shared for this research will be destroyed, because research is an ongoing process.

6. Statement of privacy rights:

- You have the right to withdraw your permission for the research doctors and participating DF/HCC entities to use or share your protected health information. We will not be able to withdraw all the information that already has been used or shared with others to carry out related activities such as oversight, or that is needed to ensure quality of the study. To withdraw your permission, you must do so in writing by contacting the researcher listed above in the section: "Whom do I contact if I have questions about the research study?"
- You have the right to request access to your protected health information that is used or shared during this research and that is related to your treatment or payment for your treatment, but you may access this information only after the study is completed. To request this information, please contact the researcher listed above in the section: "Whom do I contact if I have questions about the research study?"

Q. CONSENT TO OPTIONAL RESEARCH STUDIES:

You are being asked to participate in some optional studies. If you decide not to participate in any of the optional studies, you can still participate in the main research study. Please take your time to make your decision and discuss it with others and your primary care physician.

Your participation in these optional research studies is voluntary, and you will not be penalized or lose any benefits if you refuse to participate or decide to stop.

Optional Study #1:

If I have not yet had surgery to remove my breast cancer, I give permission to take a small tissue sample from surgery to examine my tumor for the purposes of research

Please indicate whether or not you want to take part in this optional research study.

☐ Not applicable
☐ Yes _____Initials _____Date
☐ No _____Initials _____Date

Optional Study #2:

I agree that someone may contact me in the future to ask me to take part in more research that may be relevant to me.

Please indicate whether or not you want to take part in this optional research study.

☐ Yes _____Initials _____Date
☐ No _____Initials _____Date

Optional Study #3:

I give permission for researchers to contact the person below in the event that they are unable to reach me. I will inform this person that they have been designated as the contact person in the event I cannot be reached.

Please indicate whether or not you want to take part in this optional research study.

☐ Yes _____Initials _____Date
☐ No _____Initials _____Date

Name of my designee: _____
Contact email (if known) _____
Contact phone number_____
Contact address
_____

Optional Study #4:

I would like to be contacted with a summary of the study results when they are available. I understand that I may no longer be participating on the trial or being followed at the time when results are available. Please contact me the following way(s):

- ☐ Email (provide address): _____
- ☐ Mail (provide address): _____
- ☐ Both email and mail
- ☐ Please do not contact me with this information

R. DOCUMENTATION OF CONSENT

My signature below indicates:

- I have had enough time to read the consent and think about participating in this study;
- I have had all of my questions answered to my satisfaction;
- I am willing to participate in this study;
- I have been told that my participation is voluntary and I can withdraw at any time

Signature of Participant or Legally Authorized Representative

Date

Relationship of Legally Authorized Representative to Participant

Research Consent Form
Dana-Farber/ Harvard Cancer Center
BIDMC/BCH/BWH/DFCI/MGH/Partners Network Affiliates

OHRS 11.01.2018

To be completed by person obtaining consent:

Adult Participant

The consent discussion was initiated on _____ (date).

Signature of individual obtaining consent: _____

Printed name of above: _____

Date: _____

☐ A copy of this signed consent form will be given to the participant or legally authorized representative.

☐ 1) The participant is an adult and provided consent to participate.

☐ 1a) Participant (or legally authorized representative) is a non-English speaker and signed the translated Short Form in lieu of English consent document:

As someone who understands both English and the language spoken by the participant, I interpreted and/or witnessed, in the participant's language, the researcher's presentation of the English consent form. The participant was given the opportunity to ask questions.

Signature of Interpreter/Witness: _____

Printed Name of Interpreter/Witness: _____

Date: _____

☐ 1b) Participant is physically unable to sign the consent form because:

☐ The participant is illiterate.

☐ The participant has a physical disability.

☐ Other (please describe): _____

The consent form was presented to the participant who was given the opportunity to ask questions and who communicated agreement to participate in the research.

Signature of Witness: _____

Printed Name of Witness: _____

Date: _____

☐ 2) The participant is an adult who lacks capacity to provide consent and his/her legally authorized representative:

☐ 2a) gave permission for the adult participant to participate

☐ 2b) did not give permission for the adult participant to participate