

**COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A
RESEARCH PROJECT**

**YALE UNIVERSITY SCHOOL OF MEDICINE – YALE-NEW HAVEN HOSPITAL
YALE UNIVERSITY SCHOOL OF MEDICINE – YALE-NEW HAVEN HOSPITAL:
SMILOW CANCER CENTER**

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Study Title: A Randomized Phase II trial of Neoadjuvant Cisplatin vs Doxorubicin/Cyclophosphamide (“AC”) in Women with Newly Diagnosed Breast Cancer and Germline BRCA Mutations (The INFORM:BRCA1/2 Study)

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Funding Source: Breast Cancer Research Foundation & Dana-Farber Harvard Cancer Center

Invitation to Participate and Description of Project

You are invited to take part in a clinical trial, a type of research study. You are invited to take part because you may have an inherited mutation in the BRCA1 and/or BRCA2 gene and have recently been diagnosed with breast cancer. This research study is a way of gaining new knowledge about the most effective type of chemotherapy to treat breast cancers that develop in individuals with BRCA mutations. If you decide to take part, you will be known as a “participant” rather than a “patient”. This research study is evaluating whether cisplatin, a chemotherapy agent not typically used to treat newly diagnosed breast cancer, is superior to doxorubicin and cyclophosphamide (“AC”) a standard breast cancer regimen.

It is expected that about 170 people will take part in this research study. *The sponsor is Beth Israel Deaconess Medical Center on behalf of Dana-Farber Harvard Cancer Center.* Some research studies are supported in some way by an outside organization. The Breast Cancer Research Foundation, Susan G. Komen for the Cure, Johns Hopkins University on behalf of the TBCRC, and Myriad Genetics are supporting this research study by providing funding.

This research consent form explains why this research study is being done, what is involved in participating in the research study, the possible risks and benefits of the research study, alternatives to participation, and your rights as a research participant. The decision to participate is yours. If you decide to participate, please sign and date at the end of this form. We will give you a copy so that you can refer to it while you are involved in this research study. If you choose not to participate in this research study, the research doctors will discuss other treatment options with you and/or refer you back to your regular doctor.

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WHY IS THIS RESEARCH STUDY BEING DONE?

This research study is a Phase II clinical trial. Phase II clinical trials test the effectiveness of an investigational drug, which is cisplatin in this trial, to learn how well it works in treating a specific cancer. “Investigational” means that cisplatin is still being studied for use in this setting and that research doctors are trying to find out more about it—in this case, how effective cisplatin is for treating breast cancer in BRCA mutation carriers. It also means that the FDA (the U.S. Food and Drug Administration) has not yet approved cisplatin for your type of cancer. Cisplatin has been approved by the FDA for treatment of other cancers.

The purpose of this study is to evaluate cisplatin, a chemotherapy drug that has been shown to be active in the treatment of women with breast cancer and a BRCA mutation. In this study, we are comparing cisplatin to the standard chemotherapy, doxorubicin and cyclophosphamide (“AC”) that you might receive if you did not participate in this study.

Description of Procedures

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. Tests and procedures that would be performed for your care whether you are on this study or not are referred to as “standard of care.” All of the tests and procedures listed below that will be performed at your study visits should you choose to participate in this study are standard of care unless noted with an asterisk (*) or otherwise specified.

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.

- Confirmation of your BRCA1 and/or BRCA2 mutation. If you have not had testing or your test results will not be available by the time of enrollment, BRCA1/BRCA2 testing will need to be performed.
- A medical history (questions about your health, current medications, and any allergies you may have).
- A physical exam, including vital signs and height and weight.
- Performance status, which evaluates how you are able to carry on with your usual activities.
- An assessment of your tumor by mammogram, and possibly ultrasound and MRI.
- Routine blood tests, approximately 1-2 tablespoons of blood will be collected to check your blood and assess how well your organs are functioning.
- Echocardiogram (a test that uses sound waves) or MUGA (a test in which a radioactive tracer substance is injected into your blood) to look at the function of your heart.

- Electrocardiogram (a test that uses small electrode pads) to measure the electrical activity of the heart *
- Pregnancy test, if you are a woman of child-bearing potential.
- If any of your underarm lymph nodes are enlarged on exam or by radiology studies, a fine needle aspiration (FNA) or biopsy of these lymph nodes will be performed prior to receiving chemotherapy.

If these tests show that you are eligible to participate in the research study, you will 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 after screening and before starting treatment:

- **Tumor tissue** from your original breast cancer biopsy will be obtained from your hospital and used to confirm your response to the chemotherapy that you receive. It will also be used to see if we can learn which people are likely to respond to either cisplatin or “AC”*.
- **Research biopsy:** A biopsy of your tumor tissue will be taken before you begin study treatment for research purposes. A research biopsy* is required to participate in this research study because the research done on the tumor tissue is a very important part of this research study. The researchers want to learn why some cancers shrink with this study treatment while others do not. If you do not want to have this additional biopsy, then you should not participate in the study.

A clip may be placed in the tumor bed at the time of the research biopsy, particularly if one was not placed at the time of your diagnostic biopsy. The clip is placed so that your surgeon can locate the site of the tumor at the time of surgery. This is considered a standard of care procedure for breast cancer. The research biopsy is done in an outpatient setting using a local anesthetic.

- **Research Blood sample (about 3 tablespoons):** You will have 4 additional tubes of blood collected for research purposes. Two of these tubes must be drawn prior to starting treatment and two of tubes may be collected at any time during the course of this research study. Your blood is being collected so researchers can look at your DNA. It is important to have the DNA in order to compare it to the DNA in your tumor. Your blood may also be used for future research studies*.

After the screening procedures confirm that you are eligible to participate in the research study:

Because no one knows which of the study options is best, you will be “randomized” to receive either cisplatin or doxorubicin and cyclophosphamide (“AC”) chemotherapy prior to removal of your breast cancer. Chemotherapy administered before removal of the cancer is known as neoadjuvant chemotherapy. Randomization means that you are put into a group by chance. It is

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like flipping a coin. Neither you nor the research doctor will choose what group you will be in. You will have an equal chance of being placed in either group.

Study Drugs

Cisplatin: If you are randomized to receive cisplatin you will receive cisplatin once every 3 weeks for a total of four doses. You will be given cisplatin by vein (IV) on the first day of each treatment cycle. The cisplatin infusion can take between 1 to 2 hours. Before and after receiving cisplatin, you will receive fluid hydration by vein, and you will also be given medicine to help prevent side effects such as nausea. The total time of the infusion of cisplatin and the additional fluid and medications will take about 6 hours.

After you receive cisplatin, you will be asked to drink about 12 eight ounce glasses of fluid per day, especially 2 or 3 days after therapy.

The study treatment will be stopped if you have serious side effects or if the tumor grows despite receiving cisplatin chemotherapy.

Doxorubicin and Cyclophosphamide (“AC”): If you are randomized to “AC” chemotherapy you will receive both doxorubicin and cyclophosphamide once every 2 or 3 weeks for a total of four doses by vein on the first day of each treatment cycle. The interval between chemotherapy will be decided by your research doctor. If you receive the chemotherapy every two weeks, you will also receive a subcutaneous injection the day after chemotherapy. This injection contains a medicine that contains a growth factor that will boost your immune system in order to allow your body to be ready for chemotherapy in two weeks.

The study treatment will be stopped if you have serious side effects or if the tumor grows despite the doxorubicin and cyclophosphamide chemotherapy.

Physical exams: At the beginning of each treatment cycle you will have a physical exam (including weight and vital signs) and you will be asked general questions about your health and any medications you may be taking, as well as specific questions about any side effects you may be experiencing while receiving study treatment.

Blood tests: Prior to each cycle of chemotherapy, you will have standard blood tests to check your blood counts. If you are receiving cisplatin your kidney function and body salts will also be checked prior to each chemotherapy cycle. In addition, 7-10 days after the initial four doses of the study treatment, your blood will be drawn to look at your blood cell count to determine your risk of infection; if you have received cisplatin, your kidney function and blood electrolytes will also be evaluated. The blood draw performed 7-10 days after chemotherapy can be done in the hospital where you received your chemotherapy or closer to home. About 1 tablespoon of blood will be drawn for these tests.

Surgery to Remove Your Tumor: This will occur within six weeks after the last dose of chemotherapy (either cisplatin or “AC”). Your surgery will be performed by your surgeon, as part of the standard care for your disease.

Tumor assessments: Your treating physician or nurse practitioner will examine you each time you receive chemotherapy. A measurement of your tumor will be performed on the first day of each treatment cycle as part of your physical exam.

After the tumor specimens of your initial breast cancer biopsy have been reviewed at your hospital, these tumor specimens and your tumor block will be sent to the study pathologist at Beth Israel Deaconess Medical Center. Likewise, after chemotherapy, your breast cancer will be removed by lumpectomy or mastectomy. After these tumor specimens are reviewed at your hospital, they will also be sent with the tumor block to the study pathologist so that the response of your tumor to the study treatment can be assessed. After these tumor specimens are reviewed, they will be returned to the hospital at which the biopsy and surgery were performed.

Research blood sample (about 4teaspoons): You will have 2 additional tubes of blood collected for research purposes after completing treatment. These research blood samples may be collected at any time during the course of this research study. Your blood is being collected so researchers can look at your DNA. It is important to have the DNA in order to compare it to the DNA in your tumor. Your blood may also be used for future research studies. Your blood will be stored by the study sponsor or its authorized agents until it has been exhausted. *

Additional Chemotherapy and Research Biopsy

After receiving the total course of chemotherapy, if the response in the breast cancer is not adequate before surgery, there is the option to receive additional chemotherapy outside of the trial prior to surgery. This is a decision you can make with your treating physicians. If it is determined that additional chemotherapy is needed, a second biopsy of the tumor tissue will be performed before the next chemotherapy is started*.

After Surgery (Post-Operative) Study Treatment:

Decisions about whether you will receive more chemotherapy after your surgery is up to your treating physicians. If you receive chemotherapy, the choice of chemotherapy is also up to your doctors. Decisions about post-operative chemotherapy are not part of this study.

HOW LONG WILL I BE IN THIS RESEARCH STUDY?

You will be in this research study for about 10-18 weeks. Your involvement with the study will end after your breast cancer is removed surgically.

The research doctor may decide to take you 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

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- Or for other unforeseen reasons that make it necessary to stop your participation in the research study

If you are removed from the research study, the research doctor will explain to you why you were removed. The research doctor and research team will help arrange for your continued care.

In addition, you can stop participating in the research study at any time. If you decide to stop participating in this research study, we encourage you to talk to the research doctor and your regular doctor first.

Risks and Inconveniences

There are risks to taking part in any research study. One risk is that you may get a 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 drugs 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 drugs and between individuals. For investigational drugs, not all of the risks are known at this time. **You need to tell your doctor or a member of the study team immediately if you experience any side effects.**

Since many drugs used to treat cancer are designed to cause the rapidly dividing cancer cells in your body to slow down or die, these drugs can also cause other rapidly dividing normal cells in your body to slow down or die. These include the blood cells that help to fight infection (white blood cells), the blood cells that help the blood clot (platelets), and the blood cells that carry oxygen in your body (red blood cells). When anticancer drugs cause a decrease in these blood cells, it is called bone marrow suppression. While you are participating in this research study, your blood cell levels will be monitored closely.

Please notify your doctor if any of the following occur:

- A fever of 100.5 or above.
This could be a sign of an infection. If you have a low white blood cell count, this can be serious, life-threatening or fatal. You may have to take antibiotics or be admitted to the hospital.
- Low energy or shortness of breath.
This could be a sign of anemia (not enough red blood cells). If this becomes severe, you may need to come into the clinic or hospital to have a transfusion of red blood cells.
- You bruise easily, or, when injured, you do not stop bleeding.
This could be a sign that your platelets (blood cells that help with clotting) are low. This can be serious or life-threatening. You may need to come into the clinic or hospital for a transfusion of platelets.

Many cancers are associated with an increased risk of blood clots forming that could lead to swelling in the legs and arms. These clots may travel to the lungs causing shortness of breath or

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to the brain causing a stroke. This may become serious and life threatening. Some cancer drugs can increase this risk. It is important to let your doctor know if you have increased shortness of breath or difficulty breathing.

Other common side effects include nausea, vomiting, and loss of appetite. You may also experience constipation, loose stools or diarrhea. It is important to increase your fluid intake if diarrhea occurs. If this becomes severe, you may have to be hospitalized and receive intravenous fluids.

Everyone in the research study will be watched carefully for side effects. You will be monitored during your chemotherapy 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 Cisplatin:

Common (More than 20% chance this will happen)

- Nausea, vomiting
- Infection, especially when white blood cell count is low
- Anemia which may cause tiredness, or may require blood transfusions
- Bruising, bleeding
- Kidney damage which may cause swelling, may require dialysis
- Hearing loss including ringing in ears

Occasional (Between a 4-20% chance that this will happen)

- Hair loss
- Change in taste
- Diarrhea
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Confusion
- Difficulty with balance

- Numbness and tingling of the arms and legs
Blurred vision or changes in ability to see colors (especially blue or yellow)

Rare (1-3% chance that this will happen)

- Cancer of bone marrow caused by chemotherapy later in life
- Seizure

Risks Associated with Cyclophosphamide:

Common (More than a 10% chance that this will happen)

- Hair loss
- Nausea/vomiting
- Loss of appetite
- Diarrhea
- Mouth sores
- Inflammation of the bladder with severe bleeding
- Low platelet count, which can decrease the clotting of your blood and increase your risk of bleeding and bruising.
- Low red blood cells, which carry oxygen in your body to help give you energy, which may cause tiredness (fatigue).
- Low white cell counts, which may increase the risk of 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 that can sometimes cause fatigue, muscle weakness, cramping, rigidity, irregular heartbeat or seizures. Rarely, this can be severe and possibly life-threatening and could require hospitalization and intravenous treatment.
- A blood clot. This clot 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, 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 reported include:

- Bleeding of the colon
- Inflammation of the bladder with severe bleeding
- 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
- Bladder carcinoma
- 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 Doxorubicin:**Common (More than a 10% chance that this will happen)**

- Decreased energy
- Hair loss
- Loss of menstrual cycle (amenorrhea)
- Hot flashes
- Nausea/vomiting
- Mouth sores
- Diarrhea
- Low platelet count, which can decrease the clotting of your blood and increase your risk of bleeding and bruising.
- Low red cells, which carry oxygen in your body to help give you energy, which may cause tiredness (fatigue).
- Low white cell counts, which may increase the risk of infection
- Irritation and redness of the thin membrane covering the eye

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

- Decrease in heart's ability to pump blood. The heart is not able to pump blood 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.
- Fever rash
- Skin changes
- Decreased appetite

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

- Precancerous change in the blood and bone marrow cells that lead to very low blood counts and that can turn into leukemia (blood cancer)
- Severe allergic reaction
- Irregular heartbeat that is either too fast or too slow due to abnormal electrical activity of the heart and may be life-threatening
- Sun sensitivity (photosensitivity)
- A blood clot. This clot most commonly form 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.
- 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.

- Skin and nail coloration (hyperpigmentation)
- Abnormally high levels of enzymes produced by your liver, meaning that your liver is not functioning properly and can cause fatigue, jaundice (yellowing of the skin and eyes). Although this is usually mild and reversible, this can be serious or life-threatening. Itching may occur in this situation.

Radiation Risks Associated with Scans and X-Rays:

While you are in this research study, CT scans, PET/CT scans, x-rays, mammograms, and/or other scans utilizing radioactivity may be used to evaluate your disease. In the long term, over many years, there is a very low risk of developing a new cancer as a result of the radiological evaluation and treatment for your cancer.

Risks Associated with MRI Scans:

When having an MRI (Magnetic Resonance Imaging) scan, you will lie still on a table that slides into a tunnel slightly wider than your body. People who feel uncomfortable in confined spaces (claustrophobia) may feel uncomfortable in the narrow cylinder. If you feel uncomfortable in confined spaces, please tell your research doctor. Your doctor may give you a medication to make you feel more comfortable. As images are taken, a loud banging noise will be produced. Earplugs or headphones will be available if needed. The MRI can be stopped at any time at your request, but the scan may not be complete.

Risks Associated with Biopsies:

Biopsies are normally performed under the guidance of an imaging technique. The risks may include:

- Pain and discomfort. The amount of pain and discomfort will vary, depending on the location of the biopsy site. These risks can be discussed with the study doctor.
- Minor bleeding at the biopsy site.
- Tenderness at the biopsy site.
- Scarring at the biopsy site.
- Rarely, an infection at the biopsy site.

Reproductive Risks:

The drugs used in this research study may affect a fetus. While participating in this research study, you should not become pregnant or father a baby and should not nurse a baby. Let your research doctor know immediately if you become pregnant or find out that you are going to be the father of a child. We can provide counseling about preventing pregnancy for either male or female study participants.

Fertility can be affected by the chemotherapy. Male participants may become sterile. In female participants, the menstrual cycle may temporarily be irregular, or may stop permanently resulting in an inability to become pregnant.

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.

Under some circumstances, it can be a risk for genetic information to be known by the subject or others. Variation in some genes is known to be directly related to risk of certain illnesses. In some cases, knowledge of genetic information could have negative psychological consequences or could affect access to or retention of certain benefits or entitlements. For example, the information could potentially be used against you if it were revealed to insurance companies or potential employers. However, you will not get the results of the DNA portion of the study nor will the results be made available in your medical record. Additionally, we will take precautions to ensure that confidentiality is maintained and that genetic information is not unintentionally disclosed to inappropriate third parties. There is a federal law called the Genetic Information Nondiscrimination Act (GINA) that, in general, makes it illegal for health insurance companies, group health plans, and most employers, except those with fewer than 15 employees, to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Benefits

Taking part in this research study may or may not make your health better. We hope the information learned from this research study will help doctors know how to best treat women with breast cancer and BRCA1/2 mutations in the future.

Economic Considerations

If you are considered high risks for carrying a BRCA1/BRCA2 mutation and do not have insurance coverage for testing or your test results are not available in time for enrollment, you are eligible for testing through the study. A test request form will need to be submitted to the study Sponsor to determine your eligibility for free testing.

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

You will not be paid to take part in this research study.

WHAT ARE THE COSTS?

Taking part in this research study might 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. You may be responsible for co-payments and deductibles that are typical for your insurance coverage.

Cisplatin 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 cisplatin. Doxorubicin and cyclophosphamide are approved for the treatment of early breast cancer. Therefore, you or your insurance company will be billed for the cost of these chemotherapy agents.

The additional biopsy of your tumor tissue is required as part of this research and therefore the costs associated will be covered by the study and not charged to you or your insurance company.

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:

- Yale New Haven Hospital: 203.688.2030

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 1-800-4CANCER (1-800-422-6237)

Treatment Alternatives/Alternatives

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

- Standard treatment to receive doxorubicin and cyclophosphamide “AC” but not as part of a research study
- Participation in another research study.

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

Confidentiality and Privacy

WHAT ABOUT 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. Information that does not become part of your medical record will be stored in your study

file. It may also become part of a Dana Farber/Harvard Cancer Center research database called CORIS.

The results of this research study may be published. You will not be identified in publications without your permission.

A description of this clinical trial will be available on <http://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.

PRIVACY OF PROTECTED HEALTH INFORMATION

Federal law requires Yale University 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.

Information about your study participation will be entered into your Electronic Medical Record (EMR). Once placed in your EMR, these results are accessible to all of your providers who participate in the EMR system. Information within your EMR may also be shared with others who are appropriate to have access to your EMR (e.g., health insurance company, disability provider.)

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

- Existing medical 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
- 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?

- Yale and its affiliated research doctors and entities participating in the research will use and share your protected health information. In addition, other Yale 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 Yale 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/Yale Cancer Center and its affiliates (for example, data storage companies, insurers, or legal advisors).
- The sponsor(s) of the study, its subcontractors, and its agent(s): Beth Israel Deaconess Medical Center and the Coordinating Center, Dana-Farber Cancer Institute, and Yale Cancer Center.
- Other research doctors and medical centers participating in this research, if applicable
- Your providers who are participants in the Electronic Medical Record (EMR) system
- 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 Yale 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 by telling the study staff or 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?”

WHAT HAPPENS TO MY TISSUE AND BLOOD SAMPLES?

All of the tissue and blood collected during this study will be used for research purposes only and would not be done if you were not in this study. The research on your samples may include looking at genes (DNA), proteins, or the substances that make proteins (called RNA). Collectively, this research is called biomarker research and may help doctors to better understand your disease, how the drug is working in your body, and may help to identify which people may benefit most from platinum or from doxorubicin/cyclophosphamide in the future. The research on your tumor tissue sample will not give any information on diseases that are inherited.

These tests will be performed at laboratories that may be within or outside of the study center where you received the study drug. Your tissue and blood samples will be given the same code as your other study information and kept in locked storage. Your name or other personal information will not be given to these laboratories, and only your study doctor will be able to identify you by this number. Anyone who works with your samples will hold the information and results in confidence.

If you agree the tissue and blood obtained will be stored for future research. See Future Research Studies section for more information.

In Case of Injury

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

We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

There are no plans for Beth Israel Deaconess Medical Center (BIDMC), Dana-Farber Cancer Institute (DFCI), Massachusetts General Hospital (MGH), Brigham & Women’s Hospital (BWH) or Yale University to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

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.

Voluntary Participation and Withdrawal

CAN I STOP BEING IN THE RESEARCH STUDY AND WHAT ARE MY RIGHTS?

You have the right to choose not to sign this form. If you decide not to sign this form, you cannot participate in this research study.

You can stop being 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.

If you choose not to participate, are not eligible to participate, or withdraw from this research study, this will not affect your present or future care and will not cause any penalty or loss of benefits to which you are otherwise entitled.

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 study chemotherapy. 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.

Withdrawing Your Authorization to Use and Disclose Your Health Information

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by telling the study staff or sending written notice to the study doctor, *Erin Hofstatter, MD PO Box 208092, New Haven, CT 06520-8092*. If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others until the end of the research study, as necessary to insure the integrity of the study and/or study oversight.

Questions

We have used some technical terms in this form. Please feel free to ask about anything you don't understand and to consider this research and the consent form carefully – as long as you feel is necessary – before you make a decision.

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

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Yale University, Yale Cancer Center (YCC)

- Erin Hofstatter, MD: 203-785-7309

24-hour contacts:

YCC: Erin Hofstatter, MD or your research doctor by page at 203-200-2328.

For questions about your rights as a research participant, please contact a representative of the Office for Human Research Studies at Yale University (203) 785-4688. 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.

FUTURE RESEARCH STUDIES:

What about use of my tissue and blood samples for future research?

Will I be contacted in the future about this or other research?

We may want to contact you in the future. You can decide now whether or not you want to be contacted. You can also change your mind later.

If you agree, we may contact you for several reasons. For example, over time, stored samples may be used up or decrease in quality, so we may contact you to ask for more samples. We may also contact you to update basic information or request information about your health.

Additionally, we may want to contact you to see if you want to participate in other research. We will not notify you every time your samples and information are used. However, some researchers might apply to do a study for which they would need to contact you. For example, they might want to ask you to give another sample or to fill out a survey. Or they might ask you to do a phone interview or come in to be seen by a researcher or doctor. If a study like this is approved, someone from this project will contact you. They will tell you about the study so you can decide if you want to receive more information. There will be a new consent process just for that study. You can decide then to take part or not take part. If at any time you decide you no longer want to be contacted about future studies, you can call your doctor or nurse.

Can I change my mind after I agree to let my samples be used?

You have the right to stop participating in this project at any time. If you want to leave the project, call your doctor or nurse to let us know. You will be given some options and can choose what you want us to do with your unused samples. You can also tell us to stop using your medical records. However, you cannot withdraw your samples and information from studies that have already begun. We cannot get samples and information back once they are shared with other researchers. Also, it may not be possible to remove your genetic information from scientific databases once it has been entered.

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Read each sentence below and think about your choice. After reading each sentence, choose the answer that is right for you. If you have any questions, talk to the study staff.

1. *I permit leftover samples to be stored and used for future research to learn about, prevent, or treat cancer.*

Yes No Please initial here: _____ Date: _____

2. *I permit my samples to be stored and used for future research about other health problems (for example: causes of diabetes, heart disease, and Alzheimer's, or genetic links to alcoholism).*

Yes No Please initial here: _____ Date: _____

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

Yes No Please initial here: _____ Date: _____

4. *In the event you are unable to contact me using the contact information I initially provided, I agree that someone may contact the person below in order to obtain my current contact information*

Yes No Please initial here: _____ Date: _____

Name of additional contact person: _____

Relationship (parent, spouse, child, friend): _____

Phone Number: _____

Address: _____

5. *I agree to have my coded genetic information and coded medical information placed in password-protected secured databases for research analyses.*

Yes No Please initial here: _____ Date: _____

Authorization and Permission

I have read (or someone has read to me) this form and have decided to participate in the project described above. Its general purposes, the particulars of my involvement and possible hazards and inconveniences have been explained to my satisfaction. My signature also indicates that I have received a copy of this consent form.

By signing this form, I give permission to the researchers to use [and give out] information about me for the purposes described in this form. By refusing to give permission, I understand that I will not be able to be in this research.

Name of Subject: _____

Signature: _____

Date: _____

Signature of Person Obtaining Consent

Date

Signature of Person Obtaining Consent

Date

If after you have signed this form you have any questions about your privacy rights, please contact the Yale Privacy Officer at (203) 432-5919.

If you have further questions about this project or if you have a research-related problem, you may contact the Principal Investigator Erin Hofstatter, MD at 203-785-7309. If you would like to talk with someone other than the researchers to discuss problems, concerns, and questions you may have concerning this research, or to discuss your rights as a research subject, you may contact the Yale Human Investigation Committee at (203) 785-4688.