A Phase II Randomized Trial Evaluating Neoadjuvant Dose-Dense Doxorubicin/ Cyclophosphamide Followed by Paclitaxel/Trastuzumab/Pertuzumab (AC THP) and Docetaxel/Carboplatin/Trastuzumab/Pertuzumab (TCHP) For Early Her2Neu Positive Breast Cancer
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TITLE OF RESEARCH STUDY:

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WHAT IS A RESEARCH STUDY?

A research study is when scientists try to answer a question about something that we don't know enough about. Participating may not help you or others.

People volunteer to be in a research study. The decision about whether or not to take part is totally up to you. You can also agree to take part now and later change your mind. Whatever you decide is okay. It will not affect your ability to get medical care within the Mount Sinai Health System.

Someone will explain this research study to you. Feel free to ask all the questions you want before you decide. Any new information that develops during this research study that might make you change your mind about participating will be given to you promptly.

Basic information about this study will appear on the website http://www.ClinicalTrials.gov. There are a few reasons for this: the National Institutes of Health (NIH) encourages all researchers to post their research; some medical journals only accept articles if the research was posted on the website; and, for research studies the U.S. Food and Drug Administration (FDA) calls "applicable clinical trials" 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.

PURPOSE OF THIS RESEARCH STUDY:

The purpose of this study is to determine if one chemotherapy regimen administered before surgery works better than another regimen to treat early stage Her2+ breast cancer and to determine how harmful each regimen is to the function of the heart.

Her2 positive breast cancer is a type of breast cancer that tests positive for a protein called human epidermal growth factor receptor 2 (HER2). This protein promotes the growth of cancer cells. One option for the treatment of Her2 positive breast cancer is the use of chemotherapy to shrink the breast tumor before surgery. This is called neoadjuvant chemotherapy

We will be measuring how much tumor may or may not be present at the time of surgery after 1 or 2 different regimens of chemotherapy has been given to shrink the tumor. When there is no cancer left at the time of surgery this is called a pathologic complete response (pCR). We are measuring the rates of pathologic complete response for each chemotherapy regimen.

The two chemotherapy regimens to which patients may be randomized (like the flip of a coin) are:

- **Dose Dense AC → THP** which contains doxorubicin (A), cyclophosphamide (C) every 2 weeks for 4 cycles followed by paclitaxel (T), trastuzumab (H) and pertuzumab (P) for a total of 12 weeks and
- **TCHP** which contains Docetaxel (T), Carboplatin (C), Trastuzumab (H), Pertuzumab (P) every 3 weeks for 6 cycles for total of 18 weeks.

Doxorubicin, cyclophosphamide, paclitaxel, docetaxel and carboplatin are standard chemotherapeutics. Trastuzumab and Pertuzumab are monoclonal antibodies which are specific proteins or antibodies directed against the Her2 protein or receptor on breast cancer cells. Trastuzumab and Pertuzumab are FDA approved in the treatment of Her2 positive breast cancer. Pertuzumab is a newer agent and is believed to contribute to higher rates of pCR.

You may qualify to take part in this research study because you have early stage breast cancer or inflammatory breast cancer that is Her2+ and have baseline normal heart function.

After completion of the neoadjuvant chemotherapy, **Anti-Her2 therapy will be continued on a specified schedule as per standard of care for a total of a year for BOTH regimens.**

After completion of the neoadjuvant chemotherapy you will be evaluated for surgical treatment by your breast surgeon. You will be offered surgery and radiation as determined by your breast surgeon and radiation oncologist.

After completion of surgical and/or radiation therapy, patients with estrogen receptor (ER)–positive and/or progesterone receptor (PR)–positive tumors will be offered an antiestrogen pill for further treatment of their breast cancer which is standard treatment.

Funds for conducting this research are provided by Mount Sinai.

LENGTH OF TIME AND NUMBER OF PEOPLE EXPECTED TO PARTICIPATE

Your participation in this research study is expected to last 3 years (1 year on study, 2 years of cardiac follow-up).

The study will take place in the Dubin Breast Center at Mount Sinai Hospital, Mount Sinai Beth Israel Comprehensive Cancer Center West, and Mount Sinai West.

The number of people expected to take part in this research study at MSH (Mount Sinai Hospital) is 45 patients, 18 patients at MSBI (Mount Sinai Beth Israel), and 12 patients at MSW (Mount Sinai West). The total number of people expected to take part in this research study is 75.

DESCRIPTION OF WHAT'S INVOLVED:

Research activities will take place at Mount Sinai Hospital, Mount Sinai Beth Israel and Mount Sinai West.
Screening:
After signing this consent form, you will enter the screening phase of the study during which you will have various tests and procedures to determine if you are eligible to participate in this study.

- Your medical history, height, weight, and vital signs (heart rate, blood pressure, breathing rate and temperature) will be taken. You will have a physical exam and screening echocardiogram (ultrasound of the heart) to assess the function of your heart
  Depending on the extent of lymph node involvement or abnormal lab values, imaging may be required to rule out metastatic breast cancer (cancer that has spread from the primary site [place where it started] to other places in the body) so you may also have a CT of your chest, abdomen and pelvis and bone scan or a PET/CT scan to assess the extent of disease. Your breast biopsy will confirm your cancer is Her2+ to be eligible for the study. All of this is considered standard of care.
- Approximately 3 teaspoons of blood will be taken for blood analysis. The blood will be used for a complete blood count, chemistry profile (routine lab tests looking at electrolytes and chemicals in your blood), and liver function tests. If you are a woman of child bearing age, a urine pregnancy test will be performed to ensure you are not pregnant. If you are pregnant you will be excluded from the study. All of this is standard of care.
- For Research Purposes only the following tests will be done:
  1. Performing an extra measurement on your baseline echocardiogram called longitudinal strain which is a number we will follow during the study to assess cardiac (heart) toxicity. This is done after the processing of the echocardiogram and is non-invasive. This extra measurement will not be billed to you or to your insurance.

2. Checking a baseline blood test as a marker of heart function, called troponin I (approximately a teaspoon of blood). This test will not be billed to you or to your insurance.

Once it is determined that you are eligible for the study, you will enter the treatment phase.

Study Treatment:

The study treatment you get will be chosen by chance, like flipping a coin (randomization). Neither you nor the study doctor will choose what study treatment you get. You will have an equal chance of being given each study treatment.

Arm A is for the chemotherapy treatment plan AC→ THP where A stands for doxorubicin and C stands for cyclophosphamide. This treatment is given once every 2 weeks for 4 cycles (a cycle for this regimen is 14 days). Pegfilgastrim will be administered on the second day of each cycle to boost the white blood cells to prevent infection from the chemotherapy during the AC portion. Thereafter you will receive 4 cycles (a cycle is 21 days for this portion of the treatment) of T (taxol) once weekly along with Trastuzumab and Pertuzumab (2 antibodies that target the Her2Neu receptor), given on the first day of the first week of every cycle for a total of 4 treatments. The duration of chemotherapy is approximately 20 weeks. Please see the table below.

Arm A AC →THP

	Cycle 1 14 days		Cycle 2 14 days		Cycle 3 14 days		Cycle 4 14 days		Cycle 5 21 days	Cycle 6 21 days	Cycle 7 21 days	Cycle 8 21 days	Surgery	
Visit Day	Day 1	Day 2	Day 1	Day 2	Day 1	Day 2	Day 1	Day 2	Days 1, 8, 15	Days 1, 8, 15	Days 1, 8, 15	Days 1, 8, 15		
Doxorubicin	X		X		X		X							
Cyclophosphamide	X		X		X		X							
Pegfilgastrim		X		X		X		X						
Paclitaxel									X	X	X	X		
Trastuzumab									**Day 1 only**	**Day 1 only**	**Day 1 only**	**Day 1 only**		
Pertuzumab									**Day 1 only**	**Day 1 only**	**Day 1 only**	**Day 1 only**		

AC takes approximately 3 hours to administer by infusion (a method of putting drugs into the bloodstream through a needle or catheter)
THP takes approx. 3-4 hours to administer by infusion.
Pegfilgastrim is an injection given subcutaneously (a needle applied just under the skin).

Arm B is the TCHP chemotherapy arm. Docetaxel, Carboplatin, Trastuzumab and Pertuzumab will be given on Day 1 of every 3 week cycle for 6 cycles (18 weeks). Pegfilgastrim which is administered by a subcutaneous injection will be given on the day after chemotherapy to boost the white blood cells and to prevent infections. Each administration of chemotherapy will take place at your doctor's infusion center/clinic. Please see the table below.

Arm B: TCHP

	Cycle 1 21 days		Cycle 2 21 days		Cycle 3 21 days		Cycle 4 21 days		Cycle 5 21 days		Cycle 6 21 days		Surgery	
Visit Day	Day 1	Day 2	Day 1	Day 2	Day 1	Day 2	Day 1	Day 2	Day 1	Day 2	Day 1	Day 2		
Docetaxel	X		X		X		X		X		X			
Carboplatin	X		X		X		X		X		X			
Trastuzumab	X		X		X		X		X		X			
Pertuzumab	X		X		X		X		X		X			
Pegfilgastrim		X		X		X		X				X		

TCHP takes approximately 5-6 hours to administer by infusion.
Pegfilgastrim is an injection given subcutaneously (a needle applied just under the skin)

- During each of these visits for chemotherapy, you will have a physical exam and your weight and vital signs will be taken. You will be asked about any side effects you may be experiencing, or medications you may be taking. For the duration of chemotherapy, you will be monitored via standard of care blood tests, such as hematology and, comprehensive chemistry panels (approximately 3 teaspoons of blood).
- To monitor your heart function while receiving doxorubicin or trastuzumab or pertuzumab, you will have an echocardiogram every 3 months as standard of care. And we will measure longitudinal strain which is a non-invasive mathematical measurement and is and is done post-processing as part of the experimental portion of the protocol.
- You will also have a blood test called troponin measured right before chemotherapy is administered, 24 hours after start of chemotherapy, within 1 month and 3 months of first troponin. This is part of the experimental portion of the protocol, and we will be tracking it to evaluate cardiac toxicity. The amount of blood taken for this test will be less than 1/20 of teaspoon (0.15 mL) each time.

- After completion of chemotherapy, your breast surgeon will determine the type of surgery (lumpectomy or mastectomy) or additional treatment you will undergo.
- pCR will be determine by the pathologist on the final removed tumor specimen.
- After completion of the neoadjuvant chemotherapy, **Anti-Her2 therapy will be continued on a specified schedule as per standard of care for a total of a year for BOTH regimens**
- After surgery, you may require a consultation with a radiation oncologist.
- After completion of chemotherapy and surgical and/or radiation therapy, if you are estrogen receptor (ER) positive and/or progesterone receptor (PR)positive you will be offered standard of care endocrine therapy. Tumors that are ER/PR-positive are much more likely to respond to hormone therapy which can help prevent a return of the disease by blocking the effects of estrogen.

Follow up:

- **Cardiac:** annual ultrasound of the heart will be performed for 2 years or it will be performed earlier if there is a change in symptoms.

Contraception

For Women:

Since you are participating in a study that involves drugs or investigational treatment with potential risks to a developing fetus, it is recommended, for your protection, that you not become pregnant for the duration of the study. Also, you should not participate if you are breastfeeding. Therefore, practicing effective contraception is important. No individual contraceptive is 100% effective.

Recommended methods of birth control are:

- The consistent use of an approved hormonal contraception (birth control pill/patches, rings),
- An intrauterine device (IUD),
- Contraceptive injection (Depo-Provera),
- Double barrier methods (Diaphragm with spermicidal gel or condoms with contraceptive foam),
- Sexual abstinence (no sexual intercourse) or
- Sterilization.
- If Estrogen or Progesterone receptor positive we recommend against estrogen containing oral contraceptive pills or intrauterine devices

Hormonal contraceptives, implants, and injections are only considered effective if used properly and started at least one month before you begin the study, continuing throughout the study and for one month after the end of the study. You should ask your study doctor if you should continue birth control for longer than 30 days after the end of the study. If you are unsure whether the method of birth control you use is acceptable to use while participating in this study, you should ask your study doctor before you begin the study. If you are less than one year post-menopausal, there is the potential that

you could become pregnant. If you or your partner becomes pregnant or thinks either of you may be pregnant at any time during the trial, it is important that you tell your study doctor immediately. The trial drug may be stopped and a referral will be made to an obstetrician/gynecologist for follow-up. If you plan to become pregnant in the year following a clinical trial, speak with your study doctor.

If you have any questions about birth control, your study coordinator or study doctor will be able to answer your questions and give you advice.

Should you become pregnant, regardless of the outcome, the sponsor may ask for information on your pregnancy, even if you are withdrawn from the study. Your written consent will be obtained separately in the case that this happens.

For Men:

Since you are participating in a study that involves drugs or treatment with potential risks to a developing fetus, it is recommended that you use a condom and not father a child or donate sperm while you are taking the study drug. Also, it is recommended that you use a condom and not father a child and/or donate sperm for 90 days after you stop taking the study drug. This is because levels of the study drug may be present in the sperm and/or seminal fluid even after you stop taking the study drug. Continuing to use a condom and not donating sperm during this 90 day period may allow time for any study drug that is still present in sperm and/or seminal fluid to be eliminated from your body before you attempt to father a child or donate sperm. You are encouraged to tell your female partner(s) and/or their doctor(s) that you are participating in a clinical trial.

A urine pregnancy test will be done before you begin the study.

YOUR RESPONSIBILITIES IF YOU TAKE PART IN THIS RESEARCH:

If you decide to take part in this research study you will be responsible for the following things:

- Attending study visits as specified
- Following the instructions of the study team
- Using effective birth control
- Informing the study team of new medications prescribed by any of your health providers before starting chemotherapy Informing the study team of any side effects you may experience.

COSTS OR PAYMENTS THAT MAY RESULT FROM PARTICIPATION:

Taking part in this research study may lead to added costs to you. You or your insurance company will be responsible for the costs of all items and services during the research study that you would have received for your condition if you were not enrolled in this research study. You or your insurance company will also be responsible for the costs of all services that occur during the research study that your physician believes are medically necessary to treat you.

You or your insurance company will not be responsible for the costs of the items and services associated with this research study which are provided to you only for research purposes and not to treat your condition.

You will not be paid for taking part in this study.

POSSIBLE BENEFITS:

It is important to know that you may not get any benefit from taking part in this research. Others may not benefit either. However, possible benefits may be the potential benefits of neoadjuvant chemotherapy such as shrinkage of the tumor and therefore potentially breast conserving surgery vs mastectomy as your surgical option after chemotherapy.

There is no way to predict whether a response to the study treatment will improve your quality of life or prolong survival. The results of this study may or may not help future breast cancer patients.

REASONABLY FORESEEABLE RISKS AND DISCOMFORTS:

Trastuzumab and Pertuzumab

Less Likely < 20%

- Cardiomyopathy: heart muscle becomes abnormally enlarged or thickened, decreased left ventricle ejection fraction (LVEF), fluid in the sac around the heart (pericardial effusion), inflammation/swelling of the sac around the heart (pericarditis), fast heartbeat with regular rhythm (sinus tachycardia), and fast heartbeat usually in an area above the heart's chambers (supraventricular tachycardia). We will monitor your heart function by echocardiogram every three months as standard of care.
  Diarrhea
- Fever associated with low white blood cell count
- Abdominal pain
- Mouth sores
- Nausea
- Vomiting
- Body aches
- Decreased red blood cells and increased liver proteins, these levels will be monitored during the study
- Headaches or numbness in the hands and feet can occur
- Lung inflammation (pneumonitis)
- Runny, stuff nose, sneezing or cough
- Acne
- Skin rash
- Hives

Very Unlikely < 1%

- Anaphylaxis (allergic reaction which is an abnormal reaction of the body to substances called allergens). Can cause life threatening low blood pressure, shortness of breath and death.
- Rare risk of pulmonary edema (fluid buildup in the lungs)
- Lung scarring (pulmonary fibrosis)
- This drug should not be given to anyone who has a known allergy or sensitivity to benzyl alcohol

Carboplatin:

More Likely >10%

- Peripheral Neuropathy: Tingling, numbness or pain in fingers or toes that may progress
- Electrolyte imbalances (Low Potassium or sodium for example)
- Vomiting
- Abdominal pain
- Nausea (without vomiting)
- Bone marrow depression or cytopenias of red blood cells or white blood cells or platelets thereby potentially increasing your risks of anemia, infection or bleeding
- Increased serum alkaline phosphatase, increased serum AST, these are levels of liver function
- Hypersensitivity to the medication
- Weakness
- Acute Kidney Injury

Less Likely 1% to 10%

- Hair loss
- Constipation
- Diarrhea
- Loss of taste
- Mouth sores or inflammation
- Increased serum bilirubin (one measurement of liver function)

Very Unlikely<1%

- Severe allergic reaction which is an abnormal reaction of the body to substances called allergens. Can cause life threatening low blood pressure, shortness of breath, and death.
- Loss of appetite
- Stroke
- Cardiac Failure
- Dehydration
- Redness of the skin
- Febrile neutropenia (fever in the setting of low white blood cell counts)
- High or low blood pressure
- Injection site reaction (pain, redness, swelling)
- Fatigue

- Skin rash

Doxorubicin

More Likely >10%

- Cardiomyopathy (heart muscle becomes abnormally enlarged or thickened, decreased left ventricle ejection fraction (LVEF) which is the output of blood from the heart.
- Cardiotoxicity
- Chest tightness
- Fatigue
- Headache
- Palmar-plantar erythrodysesthesia: rash that can start as redness of palms of hands and plantar aspects of feet and progress to pain and skin peeling of these areas
- Skin rash
- Kaposi sarcoma (a rare type of cancer)
- Hair Loss
- Facial swelling
- Nausea
- Constipation
- Diarrhea
- Loss of appetite
- Thrombocytopenia (low platelets)
- Neutropenia (low white blood cell count)
- Leukopenia (low white blood cell count)
- Anemia (low red blood cell count)
- Weakness
- Back pain
- Pharyngitis (throat pain or irritation)
- Dyspnea (shortness of breath)

Less Likely 1% to 10%

- Cardiac arrest
- Chest pain
- Tachycardia- accelerated heart rate
- Dizziness
- Drowsiness
- Acne vulgaris
- Weight loss
- Dehydration
- Elevated blood sugar
- Difficulty swallowing

- Inflammation or irritation of the esophagus
- Oral candidiasis (thrush or fungal infection of the mouth)
- Hematuria (blood in the urine)
- Hemorrhagic cystitis (bladder irritation resulting in blood in the urine)
- Hypersensitivity reaction
- Nose bleeds

Very unlikely < 1%

- Anxiety
- Muscle aches
- Electrolyte imbalances
- Skin rash
- Flatulence (gas)

Cyclophosphamide

More likely > 10%

- Alopecia (hair loss which may be reversible; onset: 3-6 weeks after start of treatment)
- Loss of periods
- Sterility (loss of fertility)
- Cytopenias: low red blood cell counts, low white blood cell counts that may increase risk for infection or bleeding

Less Likely: 1% to 10%

- Abdominal pain
- Anorexia (an eating disorder characterized by an abnormally low body weight)
- Diarrhea
- Mucositis (painful inflammation of the mucous membranes lining the digestive tract)
- Nausea/vomiting
- Mouth sores
- Hemorrhagic cystitis

Very unlikely < 1%

- Acute respiratory distress syndrome: accumulation of fluid in the lungs which can be severe
- High blood pressure
- Pneumonia
- Secondary malignancy
- Kidney infections
- Sepsis or systemic infections

Paclitaxel

More Likely >10%

- Flushing
- Swelling in the lower limbs
- Low blood pressure
- Hair loss
- Rash
- Nausea/vomiting
- Diarrhea
- Mouth sores or inflammation
- Neutropenia (low white blood cells)
- Anemia (low red blood cells)
- Thrombocytopenia (low platelets)
- Alkaline phosphatase increased/AST increased (measures of liver function)
- Peripheral neuropathy (tingling or numbness in fingers and toes)
- Muscle or joint aches or pains
- Weakness
- Allergic reaction
- Infection

Less Likely 1% to 10%

- Abnormal heart rhythms
- Nail changes or weakening or breaking
- Febrile neutropenia (fevers associated with a low white blood cell count)
- Bilirubin increased (a measure of liver function)

Very Unlikely <1%

- Abnormal heart rhythms
- Skin infections
- Severe allergic reaction
- Skin Rash
- Blood clots
- Pancreatitis

Docetaxel

More Likely >10%

- Flushing
- Lower limb swelling
- Low blood pressure
- Hair loss
- Rash
- Nausea/vomiting

- Diarrhea
- Mouth sores or inflammation
- Neutropenia (low white blood cells)
- Anemia (low red blood cells)
- Thrombocytopenia (low platelets)
- Alkaline phosphatase increased, AST increased (measures of liver function, require surveillance)

1% to 10%: Less Likely

- Abnormal heart rates
- Nail changes
- Febrile neutropenia (fevers associated with low white blood cells)
- Bilirubin increased (a measure of liver function)

Pegfilgastrim

More Likely > 10%

- Muscle and skeletal pain
- Limb pain

Less Likely 1-10%

- Acute respiratory distress syndrome (ARDS)
- Severe allergic reaction
- Swelling of the body
- Chest pain
- Fever
- Injection site reactions
- Rash

Other Risks

- Risk of loss of private information; this risk always exists, but there are procedures in place to minimize the risk.

Blood Draw Risks

The risks of a blood draw include pain, bruising, and the slight possibility of infection at the place where the needle goes in. Some people feel dizzy or may faint during or after a blood draw.

Fertility/Pregnancy Risks

If you are or become pregnant, this research may hurt your baby or your pregnancy in ways that are unknown. The unknown risks might be minor or might be major (death). You should not become

pregnant or father a baby while on this research study. Please read the acceptable methods of birth control found under the Description of What's Involved section of this document.

OTHER POSSIBLE OPTIONS TO CONSIDER:

You may decide not to take part in this research study without any penalty. The choice is totally up to you.
If you choose not to participate in this research study, you will continue to receive treatments and diagnostic procedures including radiographic imaging, and blood tests for your cancer that are standard of care and appropriate as determined by your medical oncologist and could potentially include either one of these treatment regimens.

IN CASE OF INJURY DURING THIS RESEARCH STUDY:

If you are injured or made sick from taking part in this research study, medical care will be provided. Generally, this care will be billed to you or your insurance in the ordinary manner and you will be responsible for all treatment costs not covered by your insurance, including deductibles, co-payments and coinsurance. This does not prevent you from seeking payment for injury related to malpractice or negligence. Contact the investigator for more information.
You are not waiving any legal right to seek additional compensation through the courts by signing this form.

ENDING PARTICIPATION IN THE RESEARCH STUDY:

You may stop taking part in this research study at any time without any penalty. This will not affect your ability to receive medical care at any of the Mount Sinai Health System hospitals or to receive any benefits to which you are otherwise entitled.

If you decide to stop being in the research study please contact the Principal Investigator or the research staff.

If you decide to stop being in the research study, the following may occur: If you were getting benefit from the study drug(s) you may experience progression off the drug and need to discuss alternative therapies with your provider.
If you stop being in the research study, already collected information may not be removed from the research study database and will continue to be used to complete the research analysis. You may be asked whether the investigator can collect information from your routine medical care. If you agree, this data will be handled the same as research data.

You may also withdraw your permission for the use and disclosure of any of your protected information for research, but you must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, the Principal Investigator for the research study may still use the information that was already collected if that information is necessary to complete the

research study. Your health information may still be used or shared after you withdraw your authorization if you have an adverse event (a bad effect) from participating in the research study.

Withdrawal without your consent: The study doctor, the sponsor or the institution may stop your involvement in this research study at any time without your consent. This may be because the research study is being stopped, the instructions of the study team have not been followed, the investigator believes it is in your best interest, or for any other reason. If specimens or data have been stored as part of the research study, they too can be destroyed without your consent. More possible reasons for removal from the study include: subjects will be removed from the research study if they become pregnant, potentially if they have tumor progression, or experience certain adverse events such as cardiac events.

CONTACT PERSON(S):

If you have any questions, concerns, or complaints at any time about this research, or you think the research has hurt you, please contact the office of the research team and/or the Principal Investigator at phone number

Icahn School of Medicine at Mount Sinai - Dr. Aarti Bhardwaj at phone number 212-824-8578

Mount Sinai Beth Israel - Dr. Paula Klein at phone number 212-604-6021

Mount Sinai West - Dr. Anupama Goel at phone number 212-523-6769

If you experience an emergency during your participation in this research, call 911 or go to the emergency room.

This research has been reviewed and approved by an Institutional Review Board. You may reach a representative of the Program for Protection of Human Subjects at the Icahn School of Medicine at Mount Sinai at telephone number (212) 824-8200 during standard work hours for any of the reasons listed below. This office will direct your call to the right person within the Mount Sinai Health System:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You are not comfortable talking to the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

DISCLOSURE OF FINANCIAL INTERESTS:

Sometimes, physicians/researchers receive payments for consulting or similar work performed for industry. Effective September 2014 Mount Sinai reviews only payments to an individual totaling more than $5,000 a year per entity when determining potential conflicts of interest. If you have questions regarding industry relationships, we encourage you to talk your physician/researcher or visit our

website at http://icahn.mssm.edu/ where Mount Sinai publicly discloses the industry relationships of our faculty.

MAINTAINING CONFIDENTIALITY – HIPAA AUTHORIZATION:

As you take part in this research project it will be necessary for the research team and others to use and share some of your private protected health information. Consistent with the federal Health Insurance Portability and Accountability Act (HIPAA), we are asking your permission to receive, use and share that information.

What protected health information is collected and used in this study, and might also be disclosed (shared) with others?

As part of this research project, the research team at the hospital(s) involved in the research will collect your: name, address, telephone, dates directly related to the individual (birth, admission, discharge, etc.), social security number, medical records number, health plan numbers, , and other unique numbers]

The researchers will also get information from your medical record at the Mount Sinai Health System and your private doctor.

During the study the researchers will gather information by:

- taking a medical history (includes current and past medications or therapies, illnesses, conditions or symptoms, family medical history, allergies, etc.)
- doing a physical examination that generally also includes blood pressure reading, heart rate, breathing rate and temperature
- completing the tests, procedures, questionnaires and interviews explained in the description section of this consent.

Why is your protected health information being used?

Your personal contact information is important to be able to contact you during the study. Your health information and the results of any tests and procedures being collected as part of this research study will be used for the purpose of this study as explained earlier in this consent form. The results of this study could be published or presented at scientific meetings, lectures, or other events, but would not include any information that would let others know who you are, unless you give separate permission to do so.

The Principal Investigator may also use and share the results of these tests and procedures to treat you in collaboration with others in the Mount Sinai Health System.

The research team and other authorized members of The Mount Sinai Health System (“Mount Sinai”) workforce may use and share your information to ensure that the research meets legal, institutional or accreditation requirements. For example, the School’s Program for the Protection of Human Subjects is responsible for overseeing research on human subjects, and may need to see your information. If

you receive any payments for taking part in this study, the Mount Sinai Finance Department may need your name, address, social security number, payment amount, and related information for tax reporting purposes. If the research team uncovers abuse, neglect, or reportable diseases, this information may be disclosed to appropriate authorities.

Who, outside Mount Sinai, might receive your protected health information?

As part of the study, the Principal Investigator, study team and others in the Mount Sinai workforce may disclose your protected health information, including the results of the research study tests and procedures, to the following people or organizations: (It is possible that there may be changes to the list during this research study; you may request an up-to-date list at any time by contacting the Principal Investigator).

- Other collaborating research center(s) and their associated research/clinical staff who are working with the investigators on this project: the Mount Sinai Hospital, Mount Sinai Beth Israel, Mouth Sinai West.
- Research data coordinating office and/or their representative(s) who will be responsible for collecting results and findings from all the centers: the Mount Sinai Hospital.
- A Data Safety Monitoring Board or other committee that will monitor the study on an ongoing basis for safety.
- The United States Food and Drug Administration.
- The United States Department of Health and Human Services and the Office of Human Research Protection.

In all disclosures outside of Mount Sinai, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier unless disclosure of the direct identifier is required by law. Some records and information disclosed may be identified with a unique code number. The Principal Investigator will ensure that the key to the code will be kept in a locked file, or will be securely stored electronically. The code will not be used to link the information back to you without your permission, unless the law requires it, or rarely if the Institutional Review Board allows it after determining that there would be minimal risk to your privacy. It is possible that a sponsor or their representatives, a data coordinating office, a contract research organization, may come to inspect your records. Even if those records are identifiable when inspected, the information leaving the institution will be stripped of direct identifiers. Additionally, when applicable, the monitors, auditors, the IRB, the Office of Human Subjects Protection (OHRP) of the Department of Health and Human Services as well as the Food and Drug Administration (FDA) will be granted direct access to your medical records for verification of the research procedures and data. OHRP and FDA are authorized to remove information with identifiers if necessary to complete their task. By signing this document you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

For how long will Mount Sinai be able to use or disclose your protected health information? Your authorization for use of your protected health information for this specific study does not expire.

Will you be able to access your records?

During your participation in this study, you will have access to your medical record and any study information that is part of that record. The investigator is not required to release to you research information that is not part of your medical record.

Do you need to give us permission to obtain, use or share your health information?

NO! If you decide not to let us obtain, use or share your health information you should not sign this form, and you will not be allowed to volunteer in the research study. If you do not sign, it will not affect your treatment, payment or enrollment in any health plans or affect your eligibility for benefits.

Can you change your mind?

You may withdraw your permission for the use and disclosure of any of your protected information for research, but you must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, the Principal Investigator for the research study may still use your protected information that was already collected if that information is necessary to complete the study. Your health information may still be used or shared after you withdraw your authorization if you should have an adverse event (a bad effect) from being in the study. If you withdraw your permission to use your protected health information for research that means you will also be withdrawn from the research study, but standard medical care and any other benefits to which you are entitled will not be affected. You can also tell us you want to withdraw from the research study at any time without canceling the Authorization to use your data.

If you have not already received it, you will also be given The Hospital's Notice of Privacy Practices that contains more information about how The Hospital uses and discloses your protected health information.

It is important for you to understand that once information is disclosed to others outside Mount Sinai, the information may be re-disclosed and will no longer be covered by the federal privacy protection regulations. However, even if your information will no longer be protected by federal regulations, where possible, Mount Sinai has entered into agreements with those who will receive your information to continue to protect your confidentiality.

If as part of this research project your medical records are being reviewed, or a medical history is being taken, it is possible that HIV-related information may be revealed to the researchers. If that is the case, the following information concerns you. If this research does not involve any review of medical records or questions about your medical history or conditions, then the following section may be ignored.

Notice Concerning HIV-Related Information

If you are authorizing the release of HIV-related information, you should be aware that the recipient(s) is (are) prohibited from re-disclosing any HIV-related information without your authorization unless permitted to do so under federal or state law. You also have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the

release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights at (888) 392-3644 or the New York City Commission on Human Rights at (212) 306-5070. These agencies are responsible for protecting your rights.

Signature Block for Capable Adult

Your signature below documents your permission to take part in this research and to the use and disclosure of your protected health information. A signed and dated copy will be given to you.

Signature of subject	Date
Printed name of subject	Time

Person Explaining Study and Obtaining Consent

Signature of person obtaining consent	Date
Printed name of person obtaining consent	Time

Witness Section: For use when a witness is required to observe the consent process,, document below (for example, subject is illiterate or visually impaired, or this accompanies a short form consent):

My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the subject, and that consent was freely given by the subject.

Signature of witness to consent process	*Date*
Printed name of person witnessing consent process	Time