CONSENT FOR CANCER RESEARCH

Project Title: CASE 13815, A phase II trial of weight-based dosing for dense weekly paclitaxel and carboplatin in overweight patients with a BSA > 2.0.

Principal Investigator: Peter Rose, MD, Cleveland Clinic 216-444-1712

Sponsor: None

Cancer research studies are coordinated by physicians and scientists from Cleveland Clinic, University Hospitals and Case Western Reserve University (CWRU) through the NIH National Cancer Institute (NCI) designated Case Comprehensive Cancer Center (Case CCC). The goal of this collaboration is to enhance cancer treatment and research in Northeast Ohio. This study is being offered at Cleveland Clinic (CC)

What is the usual approach to my gynecologic cancer?
Standard chemotherapy dosing is based on body surface area (BSA) which is the total surface area of the human body. The BSA calculation involves the height and weight of a person- meaning that the taller you are and the more you weigh increases your BSA. The average body surface area for women is about 1.6. BSA is often used when calculating doses of medications, including chemotherapy.
Many cancer studies limit the chemotherapy doses based on a BSA of 2.0. However, the number of overweight (or obese) people in the United States is increasing every year. In 2012 the American Society of Clinical Oncology (ASCO) recommended that chemotherapy dosing should be based on actual body weight for most chemotherapy drugs. Even though this recommendation was made it remains controversial. Doctors want to limit the amount and severity of side effects while at the same time giving treatment that has the most benefit in terms of survival (length of life). There has been very little research done prospectively (during the actual treatment time) that looks at this. In this study we want to look at side effects as they happen to determine if giving chemotherapy at a dose based on your actual BSA is both safe and effective.

What are my other choices if I do not take part in this study?
If you decide not to take part in this study, you have other choices. For example:
- You may choose to have the usual approach as described above
- You may choose to take part in a different study, if one is available
- Or you may choose not to be treated for cancer. For example: comfort/palliative care, which treats the symptoms of cancer, without necessarily giving chemotherapy, radiation therapy, or surgery.

Why is this study being done?
The purpose of this study is to evaluate the side effects and effectiveness of giving standard chemotherapy in doses based on your actual body surface area and not limiting the dose to BSA 2.0.

About 28 -34 people will take part in this research study at Cleveland Clinic.

What are the study groups?
All study participants will get the same study intervention. It will include chemotherapy (Paclitaxel and Carboplatin). Paclitaxel will be given at a dose based on your actual body surface area without limiting the amount given. The dose of carboplatin will be determined by a calculation that takes into account your kidney function, age, and weight. You will receive the same dose of carboplatin in this study that you would receive even if you were not in a study.

How long will I be in this study?
You will receive 6 -9 cycles of chemotherapy using Paclitaxel based on your actual body surface area plus Carboplatin at a standard dose. After completing the initial 6-9 cycles of chemotherapy, you will be asked to come back for follow up exams every 3 months for the first two years, then every 6 months for the next three years, then once yearly, depending on your clinical status.

What extra tests and procedures will I have if I take part in this study?
The exams, tests and procedures you will have are part of the usual approach for your cancer. There are no extra tests or procedures.

Before you begin the study:
You will need to have the following screening procedures performed to find out if you can be in this study. These exams and tests are part of regular cancer care and may need to be done even if you are not in the study. If you have had some of them recently they may not need to be repeated.

- History and physical examination including a measurement of your height and weight
- A review of your general health and medications (including prescription, over the counter, vitamins, and herbal or nutritional supplements) as well as any baseline symptoms you may have
- Routine blood tests (about 2 tablespoons) to check your blood counts, blood mineral levels, liver and kidney function, and a CA-125 (tumor marker that is sometimes elevated with your kind of cancer)
- Computed Tomography (CT) scans and/or Chest X-Ray to measure the size of your cancer

During the study the following will be additional procedures:
If the exams and tests show that you can be part of the study and you choose to be in the study you will have the following done:

Every cycle, Day 1 (one cycle equals 21 days) you will come to the clinic for:

- History and physical examination including a measurement of your weight
- A review of your general health and any side effects to the medication you may have

- Routine blood tests (about 2 tablespoons) to check your blood counts, blood mineral levels, liver and kidney function, and a CA-125 (tumor marker that is sometimes elevated with your kind of cancer).
- Receive chemotherapy treatment: Paclitaxel intravenously (IV) over 1 hour and carboplatin IV over 30 minutes. You will also receive medications through your IV for nausea and to help prevent an allergic reaction.

Every week (Day 8 and Day 15) you will return to the clinic for:

- Routine blood tests (about 1 teaspoon) to check your blood counts.
- Receive chemotherapy treatment: Paclitaxel IV over 1 hour and medications for nausea and to help prevent an allergic reaction.

Every 9 weeks (3 cycles) you will have a chest x-ray (or CT scan of the chest) and a CT scan of the abdomen and pelvis.

Visit	What procedures/tests will be done at this visit
Within 28 days before starting treatment	• Blood tests for CA-125 (about 1teaspoon) • History and physical examination including height and weight • Chest x-ray (or CT scan of the chest), CT scan of the abdomen and pelvis
Within 14 days before starting treatment	• Blood tests to measure blood counts, mineral blood levels, and check kidney and liver function (about 2 Tablespoons) • A review of your general health, medications as above, and any side effects to the medication you may have before starting treatment on this study.
Day 1	• History and physical examination including measurement of your weight • A review of your general health and any side effects to the medication you may have • Routine blood tests (about 2 tablespoons) to check your blood counts, blood mineral levels, liver and kidney function, and a CA-125 (tumor marker that is sometimes elevated with your kind of cancer). • IV Paclitaxel intravenously (IV) over 1 hour and carboplatin IV over 30 minutes, along with medications for nausea and to prevent allergic reactions.
Day 8 & 15	• Routine blood tests • Paclitaxel IV over 1 hour and medications for nausea and to help prevent an allergic reaction.

What possible risks can I expect from taking part in this study?

You will have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Because the dose of paclitaxel is based on your actual weight you

may have additional side effects. Side effects may be mild or very serious. We will give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the chemotherapy. In some cases, side effects can be serious because they can be long lasting, may never go away, may result in hospitalization, or may be life-threatening**.** There also is a risk of death.

The most common (more than 10%) adverse events associated with **paclitaxel** are:

- Low white blood cell counts – this may make you more prone (open) to infection
- Low platelet count – this may make you bruise more easily and bleed longer if injured
- Low red blood cell count which may cause tiredness, shortness of breath and may cause the need for a blood transfusion
- Bleeding
- Mild to severe allergic reaction which may be life-threatening with hives, wheezing and a change in blood pressure (low or high)
- Changes in the nerves that can cause numbness, tingling, or pain in the hands and feet. This may lead to difficulty walking, buttoning clothes, etc.
- Nausea and/or vomiting
- Sores in the mouth or throat (that can lead to difficulty swallowing and dehydration)
- Local swelling, redness, or skin tissue damage if some of the drug leaks from the vein while it is being given
- Diarrhea
- Hair loss
- Muscle and joint aches
- Low blood pressure that may cause lightheadedness

Less common (less than and up to 10%)

- A slowing of the heart rate (a slow pulse is not harmful; however if you should develop any other irregularities in heart rate during treatment, an EKG and other tests may be required)
- Irregular heartbeats
- Heart attack
- Increase in liver function tests that indicate your liver may not be working properly; changes in liver function can sometimes be severe
- Tiredness

The most common (more than 10%) adverse events associated with **carboplatin** are:

- Low white blood cell counts - this may make you more prone (open) to infection
- Low platelet count - this may make you bruise more easily and bleed longer if injured
- Low red blood cell count which may cause tiredness, shortness of breath or fatigue and may cause the need for a blood transfusion.

- Tiredness
- Loss of appetite and weight loss
- Diarrhea, constipation, nausea and vomiting, and abdominal pain
- Complete hair loss
- Skin rash
- Changes in taste
- Changes in electrolytes and minerals in the blood such as magnesium, potassium, sodium, and calcium

Less common (less than and up to10%)

- Changes in the nerves that can cause numbness, tingling, or pain in the hands and feet
- Mild to severe allergic reaction which may be life-threatening with hives, wheezing and low blood pressure
- Hair loss
- Ringing in the ears and hearing loss
- Other sensory side effects (for example: visual disturbances or changes in taste)
- Abdominal pain, diarrhea, or constipation
- Decrease in kidney (if severe, dialysis might be necessary) or liver function

CT scans:
If you take part in this research, you will have one or more medical imaging studies which use radiation. The radiation dose we have discussed is what you will receive from this study only, and does not include any exposure you may have received or will receive from other tests. The CT scan that you will receive in this study will expose you to low amounts of radiation. Every day, people are naturally exposed to low levels of radiation that come from the sun and the environment. This type of radiation is called "background radiation." No one knows for sure whether exposure to low amounts of radiation is harmful for your body. However, scientists believe that being exposed to too much radiation can cause harmful side effects, including causing a new cancer. The amount of radiation that scientists think can cause harmful side effects equals more than 15 times the amount of extra radiation you would receive from being in this study. Also, scientists believe the number of people who would be at risk for developing a second cancer from being exposed to large amounts of radiation to be about 1 out of every 1,000.

Blood Draws:
The insertion of the needle to draw blood is painful; however, the discomfort is brief. For most people, needle punctures to get blood samples do not cause any serious problems; however, they may cause bleeding, bruising, discomfort, infections, dizziness, or fainting.

Reproductive Health/Sexual Activity
You should not get pregnant or breastfeed, a baby while in this study. The chemotherapy used in this study could be very damaging to an unborn baby. Check

with the study doctor about what types of birth control, or pregnancy prevention, to use while in this study.

What possible benefits can I expect from taking part in this study?
We cannot know if you will have any benefit as a result of your participation in the study; it is possible the study treatment may improve your cancer, which may give you relief from some symptoms, improve your quality of life or prolong your survival. However, it is possible that your condition could worsen. Your participation in this study will help to obtain information about treating subjects with gynecologic cancer in the future.

Can I stop taking part in this study?
Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:
- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study requirements
- If the study is stopped by the doctors involved with the study, Institutional Review Board (IRB) or FDA.
- If you get pregnant.

What are my rights in this study?
Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

What are the costs of taking part in this study?
Your involvement in this research study is voluntary and you will not be paid for your participation.

You and/or your health plan/insurance company will need to pay for all of the costs of treating your cancer in this study (i.e., physical exams, routine blood tests, pregnancy test, x-rays and/or scans for tumor measurement, as well as the cost of any medicines to manage the side effects of treatment).

The costs of the chemotherapy drugs paclitaxel and carboplatin as well as the costs of administering these treatments will be billed to your health plan or insurance company. If your insurance plan/company denies payment for the costs of and treatment with these chemotherapy drugs, you will be held responsible for covering these costs.

Some health plans will not pay these costs for people taking part in studies. Before you decide to be in the study you should check with your health plan or insurance company to find out what they will pay for. You may also ask to speak with a financial counselor for specific insurance plan deductible/co-payment obligations. Taking part in this study will may or may not cost your insurance company more than the cost of getting regular cancer treatment. You will be responsible for paying any deductibles, coinsurance, and co-payments as required under the terms of your insurance plan(s).

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://www.cancer.gov/clinicaltrials/learningabout.

What happens if I am injured or hurt because I took part in this study?
If you believe that you are injured as a result of the research procedures being performed, please immediately contact the study doctor.

If injury occurs as a result of your involvement in this research, medical treatment is available from Cleveland Clinic or another medical facility but you/your medical insurance will be responsible for the cost of this treatment. A research injury is an injury that happens as a result of taking part in this research study. If you are injured by a medical treatment or procedure that you would have received even if you weren't in the study that is not considered a "research injury". There are no plans for payment of medical expenses or other payments, including lost wages, for any research related injury. To help avoid injury, it is very important to follow all study directions.

Further information about research-related injuries is available by contacting the Cleveland Clinic Institutional Review Board at (216) 444-2924.

HIPAA AUTHORIZATION
Authorization to Use or Disclose (Release) Health Information that Identifies You for a Research Study

If you volunteer to participate in this research, your protected health information (PHI) that identifies you will be used or disclosed to Dr. Peter Rose and the research study staff at Cleveland Clinic for the purposes of this research and to Case Western Reserve University for administration.

The PHI that we may use or disclose (release) for this research may include your name, address, phone number, date of birth, Social Security number, information from your medical record, lab tests, or certain information relating to your health or condition.

Some of the tests and procedures done solely for this research study may also be placed in your medical record so other doctors know you are in this study. Upon completion of the study, you may have access to the research information that is contained in your medical record.

In addition to the investigators and research staff listed above, your PHI may be looked at by other groups involved with the study such as the Cleveland Clinic Institutional Review Board, and the Case Comprehensive Cancer Center Protocol Review and Monitoring Committee. Your PHI may also be used by and/or disclosed (released) to:

- Case Comprehensive Cancer Center members and collaborators
- The Food and Drug Administration;
- The Department of Health and Human Services;
- The National Cancer Institute (NCI);

Once your personal health information is released it may be re-disclosed and no longer protected by privacy laws.

Your research information may be used and disclosed indefinitely, but you may stop these uses and disclosures at any time by writing to:

Peter Rose, MD
Case Comprehensive Cancer Center
Cleveland Clinic
9500 Euclid Avenue/A81
Cleveland, OH 44195

Your participation in the research will stop, but any information previously recorded about you cannot be removed from the records and will continue to be used as part of this research. Also, information already disclosed outside the Cleveland Clinic cannot be retrieved. This will not affect your rights to treatment or benefits outside the research study.

The Cleveland Clinic will not use your information collected in this study for another research purpose without your written permission; unless the Cleveland Clinic Institutional Review Board (IRB) assures your privacy and confidentiality is protected. The IRB is a committee whose job it is to protect the safety and welfare of research subjects.

By signing this informed consent form, you are authorizing such access to your research and medical record information. If you choose not to sign this consent form, you will not be able to participate in this research study. This Authorization does not have an expiration date.

Voluntary Participation
Your participation in this research study is voluntary. Choosing not to participate will not alter your usual health care or involve any penalty or loss of benefits to which you are otherwise entitled. If you decide to join the study, you may withdraw at any time and for any reason without penalty or loss of benefits. If information generated from this study is published or presented, your identity will not be revealed.

In the event new information becomes available that may affect the risks or benefits associated with this study or your willingness to participate in it, you will be notified so that you can decide whether or not to continue participating.

Questions about the Research
If you have any questions, you can ask the Principal Investigator and/or research staff at Cleveland Clinic (216) 444-1712).

Emergency or after-hours contact information

Since you are a **Cleveland Clinic Main Campus patient**, you should contact the page operator at (216) 444-2200 or toll free at (800) 223-2273, and ask for the oncologist (cancer doctor) that is on call.

If you are a **Cleveland Clinic-Fairview patient**, please call (216) 476-7540

If you are a **Cleveland Clinic-Hillcrest patient**, please call (440) 312-5560.

Where Can I Get More Information?
If the researchers cannot be reached, or if you would like to talk to someone other than the researcher(s) about: concerns regarding the study, research participant's rights; research-related injury; or other human subjects issues, you may contact the Institutional Review Board (IRB) at Cleveland Clinic IRB 216-444-2924

You may call the National Cancer Institute's Cancer Information Service at: 1-800-4-CANCER (1-800-422-6237)

You may also visit the NCI Web site at http://cancer.gov/

- For NCI's clinical trials information, go to: http://cancer.gov/clinicaltrials/
- For NCI's general information about cancer, go to http://cancer.gov/cancerinfo/

You will get a copy of this form. If you want more information about this study, ask your study doctor.

US National Institutes of Health (NIH) Clinical Trial Database:
A description of this clinical trial will be available on http://www.ClinicalTrials.gov, if applicable, 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.

12. Signature

Signing below indicates that you have been informed about the research study in which you voluntarily agree to participate; that you have asked any questions about the study that you may have; and that the information given to you has permitted you to make a fully informed and free decision about your participation in the study. By signing this

consent form, you do not waive any legal rights, and the investigator(s) or sponsor(s) are not relieved of any liability they may have. A copy of this consent form will be provided to you.

Signature of Participant	**Date**	**Printed Name of Participant**

I have discussed the information contained in this document with the participant and it is my opinion that the participant understands the risks, benefits, alternatives and procedures involved with this research study.

Signature of Person Obtaining Consent	**Date**

Printed Name of Person Obtaining Consent