ID: UMCC 2017.113

Individualized Adaptive De-escalated Radiotherapy for HPV-related Oropharynx Cancer

NCT03416153

UNIVERSITY OF MICHIGAN
CONSENT TO BE PART OF A RESEARCH STUDY

1. KEY INFORMATION ABOUT THE RESEARCHERS AND THIS STUDY

Study title: (UMCC 2017.113) A Multi-Center Phase II Trial of Individualized Adaptive De-escalated Radiotherapy Using Pre and Mid-Treatment FDG-PET/CT for HPV-related Oropharynx Cancer

Company or agency sponsoring the study: University of Michigan Radiation Oncology

Principal Investigator:

Michele Mierzwa, MD, Department of Radiation Oncology, University of Michigan

1.1 Key Study Information

You may be eligible to take part in a research study. This form contains information that will help you decide whether to join the study. All information in this form is important. Take time to carefully review this information. After you finish, you should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others such as your friends, family, or other doctors about your possible participation in this study. If you decide to take part in the study, you will be asked to sign this form. Before you do, be sure you understand what the study is about.

2. PURPOSE OF THIS STUDY

2.1 Study purpose:

The purpose of this study is to see if pre-treatment and mid-treatment PET-CTs can be used as markers or guides to adapt the amount of radiation therapy given in combination with chemotherapy to patients with HPV-related squamous cell carcinoma of the oropharynx. In this study, if the mid-treatment PET-CT shows that the protocol specific parameters are met, the total radiation given will be reduced (54 Gy over 27 fractions). If the mid-treatment PET-CT shows that the protocol specific parameters are not met, the total radiation therapy given will remain at the standard of care dose (70 Gy over 35 fractions).

3. INFORMATION ABOUT STUDY PARTICIPANTS (SUBJECTS)

Taking part in this study is completely **voluntary**. You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

3.1 Who can take part in this study?

Patients with squamous cell carcinoma of the oropharynx (tonsil, base of tongue, oropharyngeal wall, soft palate) that is p16 positive or HPV positive are able to participate in this study.

There are many other inclusion and exclusion criteria which the doctors will use to determine if you can participate in this study. It is important that you discuss your full medical history and all of your medications with your doctor.

3.2 How many people (subjects) are expected to take part in this study?

A total of approximately 92 subjects at several institutions will take part in this study, including approximately 82 subjects from the University of Michigan.

4. INFORMATION ABOUT STUDY PARTICIPATION

4.1 What will happen to me in this study?

The study team will explain the research study and answer any questions you have about the study. If you want to participate in the study, the study team will request you sign the consent form prior to any activities occurring that pertain to the study. Once your consent is obtained, the study team will look through your medical chart, ask

you questions, and begin scheduling tests and procedures to determine if you are eligible for the study. The study team will inform you of the types of tests and procedures required before the study begins.

Many of the procedures that will be performed during the study, including routine blood tests, tumor evaluations (radiology scans), physical examinations, vital signs (blood pressure, heart rate, breathing rate, and temperature) and measurement of height and weight, would normally be done as part of your standard of care regardless of study participation. However, some of these may be done more frequently as a result of your participation in this study. One PET-CT, and some blood sample collection and analysis are solely for research purposes. Tests and procedures that are done more often than your regular medical care because of your study participation and that are solely for research purposes will be identified below. The study staff will inform you of the types of tests and procedures you have to undergo during the study.

During the study you must:

- Follow the instructions you are given.
- Come to the study center for your visits or complete virtual study clinic visits with the study doctor.
- Tell the study doctor or study staff about any changes in your health and/or medications you are taking.
- Tell the study doctor or study staff if you want to stop being in the study at any time.

Before starting the study:

You will need to have the following exams, tests or procedures to find out if you can be in this study. If you have had some of them recently, they may not need to be repeated. The screening tests and procedures do not have to be completed in one day and you are allowed to take breaks if you have multiple procedures in one day.

Before you begin the study you will need to have the following **screening procedures**:

- **Medical history**: including any past treatments, surgeries, infection, autoimmune diseases and smoking history.
- **Medications**: It is important that you tell your doctor about all of the medications that you have been taking, including over the counter medicines, vitamins or herbal treatments.
- **Physical exam**: including measurement of your height, weight, blood pressure, heart rate, respiratory rate and temperature. Vital signs are allowed to be measured by you and your family without coming to the study clinic.
- **Performance status**: Your ability to perform day to day activities and care for yourself
- **Routine blood tests (approximately 2 teaspoons)**: will be drawn for tests to check blood counts and chemistry
- **Scans of your cancer**:
    - Computed tomography (CT) of the neck and chest. Additional scans (CT of the abdomen/pelvis and/or bone scan) could be performed if your treating doctor feels they are necessary.
        - A CT scan uses special x-ray equipment to make detailed pictures of body tissues and organs. For the CT scan, you may be given a “contrast material” (a special dye that makes it easier for doctors to see different tissues in your body). You will be asked to lie still and may be asked to hold your breath for a few seconds. The CT scan is done in the Radiology Department and takes about half an hour.
    - Magnetic Resonance Imaging (MRI) scan takes an image of your head or body to observe the location and size of your tumor. For the MRI scan, you may be given a “contrast material” (a special dye that makes it easier for doctors to see different tissues in your body). You will be asked to lie down on a narrow bed which will slide into a tunnel that is 6 feet long by 22 inches across and is open at each end. You will be asked to lie quietly for about one hour, during which time you will hear a loud machine-like noise. A MRI scan takes about an hour and a half to complete.

- **Videofluoroscopy**: to evaluate swallowing problems from radiotherapy, you will undergo an evaluation of swallowing by videofluoroscopy (VF). VF consists of swallowing a small quantity of barium, or a barium-coated food such as a cookie, while a series of x-rays are taken of the throat. When staff is not available, the videofluoroscopy will be skipped.
- **Dental exam**
- **Nutritional assessment**
- **The following will be done for research purposes:**
  If the exams, tests and procedures show that you can take part in the study, and you choose to take part, then you will have the following extra screening procedures:
    - Approximately 2-3 teaspoons (12 mL) of blood will be drawn for biomarker tests (substances in your blood, such as proteins). Measuring biomarkers in the blood could help predict whether or not someone is likely to benefit from a therapy.
    - Quality of life questionnaires; you are free to skip any questions that you would prefer not to answer. You can complete these questionnaires at home and mail, fax, or send them through the patient portal to the study clinic.
    - Tumor biopsy submission – evaluation of tumor tissue that was already taken; this will include genetic testing
    - PET-CT
        - PET-CT scan uses xray equipment and a contrast dye that detects areas of high metabolic activity (cancer has a high metabolic activity).

Treatment

You will start out receiving standard chemoradiation which includes carboplatin and paclitaxel, intravenously (meaning it's given through a vein in your arm) on a weekly schedule at the same time as radiation therapy for a total of 6-7 doses and 70 Gy in 35 fractions.

You will undergo a mid-treatment PET-CT and MRI between radiation therapy fraction 8 and 12. If your PET-CT parameters **meet the criteria** for de-escalation, you will have your standard chemoradiation decreased as follows: radiation therapy will be changed to 54 Gy total dose and only 6 doses of carboplatin and paclitaxel at the same time as radiation therapy.

If you PET-CT parameters **do not meet the criteria** for de-escalation, you will continue your standard chemoradiation as described above.

While you are receiving the chemoradiation, you will have the following weekly tests and procedures (virtual or in-person):

- Physical exam
- Routine blood tests to check blood counts and chemistry
- Medication review
- Toxicity evaluation: You will be asked about any side effects or illnesses you experience

The following tests will be done weekly for research purposes only:

- Approximately 2-3 teaspoons (12 mL) of blood will be drawn for biomarker tests. For certain visits, blood draws may be skipped based on the availability of the local lab.
- Quality of life questionnaire; you are free to skip any questions that you would prefer not to answer.

Follow-up

You will be asked to return to the clinic or complete virtual clinic visits for check-ups at 1 month after completion of therapy and then every 3 months for a total of 2 years.

You will have the following tests and procedures during follow-up (virtual or in-person):

- Physical exam
- Medication review
- Toxicity evaluation
- Videofluoroscopy – 3 month and 12 month only (if staff available)
- PET/CT – 3 month only

The following tests will be done in follow-up (through 1 year) for research purposes only:

- Approximately 2-3 teaspoons (12 mL) of blood will be drawn for biomarker tests.
- Quality of life questionnaires; you are free to skip any questions that you would prefer not to answer.

OPTIONAL Research Samples Stored for Future Use:

Besides the information about the main study, the following information is specific to unspecified future use of identifiable data and/or biospecimens. We would also like your permission to keep some of your blood, tumor tissue, and medical information collected in the main study, so that we may study it in future research. The future research may be similar to this study or may be completely different.

You can take part in the main study even if you decide not to let us keep your blood, tumor tissue, and medical information for future research.

If you give us permission, we will use your blood, tumor tissue, and medical information for future research. Even if you give us permission now to keep some of your blood, tissue, and medical information, you can change your mind later and ask us to destroy it. Keep in mind, however, that once we have analyzed your blood tissue, we may not be able to take the information out of our research.

We may share your blood, tumor tissue, and medical information with other researchers, so that they can use it in their research. Their research may be similar to this study or may be completely different. Once we have shared your blood, tissue and medical information with other researchers, we will not be able to get it back. Future use of your identifiable data and/or specimens will be conducted in compliance with applicable regulatory requirements.

You will not find out the results of future research on your blood and tissue samples. Allowing us to do future research on your blood, tissue and medical information will not benefit you directly.

With appropriate permissions, your samples and collected information may also be shared with other researchers here, around the world, and with companies.

Your identifiable private information or identifiable biospecimens may be stripped of identifiers and used for future research studies or distributed to another researcher for future research studies without additional informed consent.

Research can lead to new discoveries, such as new tests, drugs, or devices. Researchers, their organizations, and other entities, including companies, may potentially benefit from the future research on your blood, tumor tissue, and medical information. You will not have rights to these discoveries or any proceeds from them.

You can make your choice about whether to participate in the Optional substudy (storage of research samples for future use) in Section 12 of the consent.

Refer to Section 5.1 below for any additional risks as well as efforts to minimize the risks, such as the GINA statute (Section 9.1) for the research samples stored for future use substudy.

Loss of Confidentiality
Your samples will be coded however there is a risk of loss of confidentiality of your information. If your samples are provided to research collaborators the following information may be made available: your diagnosis and treatments, the time the samples were collected in relation to your study regimen, your disease status, and demographic data (for example gender, race, age, etc.). Please ask the Study Doctor or Study Nurse if you would like to know more about how your information will be protected.

4.2 How much of my time will be needed to take part in this study?
Typically, a course of radiation lasts 6-7 weeks and treatments are delivered each day, Monday through Friday, each week. Each radiation treatment lasts approximately 10-20 minutes. Carboplatin and paclitaxel infusion will require a couple hours once weekly during this time period.

Follow-up visits last about 1 hour each and may be completed virtually.

4.3 When will my participation in the study be over?
After your radiation treatment is completed, you will return for follow-up appointments one month after treatment, then every 3 months for up to 2 years.

4.4 What will happen with my information and/or biospecimens used in this study?
You collected information and biospecimens may also be shared with other researchers, both here or around the world, or with companies. Any sharing is subject to contractual obligations with the Sponsor. Additionally:

- With appropriate permissions, your identifiable collected information and biospecimens may be shared, and/or,
- Without your additional consent, your identifiable private information and identifiable biospecimens may be stripped of identifiers and used for future research studies or distributed to another researcher for future research studies.

5. INFORMATION ABOUT RISKS AND BENEFITS

5.1 What risks will I face by taking part in the study? What will the researchers do to protect me against these risks?
The drugs used in the study may cause certain side effects and discomforts. You may have all, some, or none of the known side effects. There is also a risk that other rare or unknown side effects may occur. Your doctors and nurses will check you closely for side effects, and may give you medicines or other treatments to stop or reduce some of these effects. Some side effects may go away soon after the study medication is stopped, but in some cases, side effects may be serious, long lasting, and/or permanent. There is even a chance that a side effect may cause death. If you have any side effects, it is important that you report them to your study doctor or research staff.

These risks will be minimized by monitoring you carefully. We will provide the usual supportive care that would be routinely given to someone with your condition. If you have side effects from the study intervention,

we will make appropriate adjustments as defined by the study protocol. You may need to discontinue the study intervention if the side effects are too serious.

The known or expected risks are:

Risks and Side Effects Related to Radiation Therapy of the Oropharynx

Very Likely (10-25% of subjects)

- Sores in the mouth and/or throat which can be painful and make it very difficult to chew and or swallow foods
- Mouth dryness or changes in taste and/or smell that may be permanent
- Hoarseness
- Tanning or redness and/or irritation of the skin in the head and neck area being treated with radiation
- Ear pain and/or pressure
- Fatigue
- Weight loss
- Permanent hair loss in the area treated with radiation (face, chin, neck)
- Loss of teeth, or cavities in the teeth, if strict dental care is not followed and/or hypersensitivity of teeth

Less Likely, But Serious (1-9% of subject; except if noted)

- Decrease in function of the thyroid gland that may require you to take thyroid replacement medicine to prevent you from feeling tired or sleepy
- Damage to nerves in the neck, jawbone, voice box, skin, or other parts of the head and neck that may require a major operation to correct and, rarely, can even be life threatening (1-5% of subjects)
- Temporary pain or scarring around nerves in the shoulder that could cause numbness and/or weakness
- Breathing problems
- Difficulty with swallowing and eating for which you might need a long term or permanent feeding tube; possibility of inhaling food and/or liquids into the lungs – which could also result in pneumonia.
- Serious ear infections and/or hearing loss

Rare but very serious (< 1%)

- Damage to the spinal cord
- Damage to carotid arteries leading to permanent weakness and/or symptoms like a “stroke.” Stroke ≥ 5 years after radiation has been reported to be slightly higher after head and neck radiation, compared with the general population, due to the possibility of increased formation of plaque in the carotid artery (causing blockage).

All these side effects may be a result of standard radiation treatment, as well as radiation according to this study. Your physicians do not know whether the chance of complications arising from participation in this study is different from the chance of complications arising from standard radiation.

Risks and Side Effects Related to Carboplatin

COMMON, SOME MAY BE SERIOUS In 100 people receiving Carboplatin, more than 20 and up to 100 may have:
• Hair loss • Vomiting, nausea • Infection, especially when white blood cell count is low • Anemia which may cause tiredness, or may require blood transfusions • Bruising, bleeding • Belly pain

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Carboplatin, from 4 to 20 may have:
• Diarrhea, Constipation • Numbness and tingling in fingers and toes • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Changes in taste • Changes in vision

RARE, AND SERIOUS In 100 people receiving Carboplatin, 3 or fewer may have:
• Damage to organs which may cause hearing and balance problems

Risks and Side Effects Related to Paclitaxel

COMMON, SOME MAY BE SERIOUS In 100 people receiving Paclitaxel, more than 20 and up to 100 may have:
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Infection, especially when white blood cell count is low • Bruising, bleeding • Anemia which may cause tiredness, or may require blood transfusions • Pain • Sores in mouth which may cause difficulty swallowing • Diarrhea, nausea, vomiting • Muscle weakness • Numbness, tingling or pain of the arms and legs • Hair loss

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Paclitaxel, from 4 to 20 may have:
• Abnormal heartbeat • Blood clot which may cause swelling, pain, shortness of breath • Damage to the lungs which may cause shortness of breath

RARE, AND SERIOUS In 100 people receiving Paclitaxel, 3 or fewer may have:
• Heart attack or heart failure which may cause shortness of breath, swelling of ankles, and tiredness • A tear or a hole in the bowels which may cause pain or that may require surgery • Severe skin rash with blisters and peeling which can involve mouth and other parts of the body

Risks of Blood Draw

Collection of blood samples may cause pain, bleeding, bruising or infection. It is also possible that you may feel lightheaded or faint. Please tell your study doctor or the study nurse if you do not feel well after having your blood drawn at any time during your study participation.

Risks of Questionnaires

There is a risk you will be asked questions that you find uncomfortable. You have the right to refuse to answer any question.

Risks of CT Scan

The contrast substance injected during the CT scan may cause pain, burning feeling, sweating and rarely an allergic reaction that can be serious. If you know you're allergic to iodine; you must inform your doctor immediately. The contrast agent used in the CT scan may cause kidney damage, especially if you're diabetic, dehydrated and if you're older. In addition, your thyroid function may be affected.

CT imaging uses ionizing radiation, which increases your risk of cancer. Everyone is exposed to naturally occurring ionizing radiation every day. The amount of radiation exposure from 1 CT scan is approximately comparable to 1-3 years of natural background radiation.

PET/CT scanning using [18F]FDG and Diagnostic CT scan. PET/CT scanning is associated with several risks, as follows:

Intravenous line (IV) for radiotracer injections: There is an infrequent risk of bruising, bleeding, infection, or soreness associated with intravenous catheter placement, similar to the risks associated with routine blood testing. Subjects might feel dizzy or lightheaded or may rarely even faint when the tube is put in or taken out. The risk of these side effects is minimized by using highly trained personnel.

Low-level Radiation Exposure: During the course of this study, subjects will be exposed to radiation from the PET radiotracer 2-[18F]fluoro-2-deoxy-D-glucose ([18F]FDG), a radioactive form of sugar. The biological effect of radiation exposures is measured in milli-Sieverts (mSv), which is a unit of whole body radiation exposure, called the 'effective dose'. The effective dose from the [18F]FDG injected into your bloodstream is 5.6 mSv, and the effective dose from the CT scan taken at the same time is 5.8 mSv, for a total effective dose of 11.4 mSv.

The effects on your body of this radiation exposure will be added to your overall life-time radiation risk. Your life-time radiation risk includes the background radiation you are exposed to naturally like everyone else living on this planet, which averages 3 mSv per year. The radiation you will be exposed to in this study is about 4 times the yearly background radiation. In terms of radiation a person may get exposed to during medical care, the amount you will receive in this study will be less than 2 times the amount of radiation received in a CT scan of the chest, which is about 8 mSv. The Federal Government requires that the amount of radiation exposure of radiation workers does not exceed 50 mSv per year; the radiation you will be exposed to from PET/CT scans in this study is about 22% of that amount. Your life-time radiation risk also includes any radiation you may have received in the past for diagnosis or treatment, and any such radiation you may be exposed to in the future. The risk from radiation exposure of this amount is considered to be similar to other every day risks, such as driving a car. No PET studies will be performed on pregnant, nursing, or potentially pregnant women, as determined by pregnancy testing within 48 hours prior to the PET scanning session.

The researchers will try to minimize the risks (above) by:

PET/CT and CT scanning: Skilled nuclear medicine technologists will perform the PET/CT and CT studies under the supervision of a physician who is a specialist in nuclear medicine. We will use aseptic techniques and highly trained personnel to minimize the risks associated with venipuncture (IV). A physician or nurse will be available at all times during the study, and any adverse reactions will be treated immediately. A fully equipped medical cart is located in the PET facility. No PET studies will be performed on pregnant, nursing, or potentially pregnant women, as confirmed by pregnancy testing (b-HCG) performed within 48 hours prior to each PET scanning session for women of childbearing potential.

Risk to embryo or fetus:

If appropriate, you will be asked if there is a possibility that you may be pregnant. You may not take part in this project if you are pregnant. If you are or may become pregnant, this research may involve unforeseeable risks to you, the embryo, or the fetus.

To minimize this risk, sexually active women with child-bearing potential must be using adequate contraceptive measures. If there is a question of pregnancy, a pregnancy test will be done.

Risks and Side Effects Related to MRI

MRIs done for research that use IV contrast have risks similar to MRIs done for clinical care. Contrast is used to improve the pictures of the inside of the body made by the MRI. Common risks of MRI include: feeling fearful of being in a small enclosed space (claustrophobia) when you are lying inside the MRI scanner, feeling uncomfortable because of the loud noises made by the machines, and feeling uncomfortable with the physical sensations you may feel during the process. You are also exposed to some risk because of the injected contrast, gadolinium-DTPA, which may cause headache, nausea, and local burning sensation.
The contrast agent, gadolinium has been linked to development of Nephrogenic Fibrosing Dermopathy (NFD), also known as Nephrogenic Systemic Fibrosis (NSF). NFD is a thickening of the skin, organs and other tissues and is a rare complication in subjects with kidney disease who undergo an MRI with contrast material. To help prevent this, we will check how well your kidneys work before you have any MRIs. Because of the use of contrast, all female subjects who are able to have children will be required to use adequate birth control. If you have implanted metal objects such as a pacemaker, artificial limbs, or metal joints, you will not be able to have an MRI done, and may not be able to take part in this research.

Reproductive Risks

WOMEN

There could be risks to a fetus in this study. If you are pregnant or become pregnant during the study, these risks could affect you or your fetus. Women must agree to either abstain from sexual activities that could result in pregnancy or use at least one acceptable method of birth control (i.e. condom, IUD, pill) while taking part in this study.

MEN

Men must agree to either abstain from sexual activities that could result in pregnancy or use an acceptable form of birth control while taking part in the study Acceptable forms of birth control are male latex condom (with or without spermicide) or vasectomy.

Risk Reduction:

Your doctor will see you on a weekly basis during treatment to assess the side effects. Physical examinations, scans and other routine tests will be done to monitor the effects of the treatment. Although many side effects disappear after radiation therapy has been completed, some are permanent. You understand that you may ask your doctor about these side effects. You will be informed about ways to minimize sore mouth and throat during radiation therapy, including rinsing the mouth with salt and soda solutions, taking appropriate pain medication and other measures which will be given to you by your nurses and doctors as necessary. Close follow-up will be performed after radiation is completed, to assess any long-standing side effects of radiation.

Before each treatment of carboplatin and paclitaxel you will receive standard medications to decrease the chances that you will experience nausea, vomiting, and an allergic reaction. These medications will be determined by your medical oncologist. Your heart rate and blood pressure will be monitored during your carboplatin and paclitaxel treatments. Because fever is a sign of infection, and you will be at an increased risk for infection during therapy, it is important that you contact your physician if you develop a fever during treatment in order that appropriate treatment can be started. Frequent blood samples will be taken to monitor the number of white blood cells, red blood cells, and platelets you have in your blood to monitor how the treatment is affecting your body. If your body can not make enough white blood cells, red blood cells, and platelets due to the treatments, your physician will begin appropriate treatment. If you develop severe redness of your skin or pain in your mouth and throat your physician may temporarily hold or modify your carboplatin and paclitaxel treatment. If you are able to resume carboplatin and paclitaxel, you may be given a lower dose of the medication(s) in order to decrease the risk of redness of your skin and pain in your mouth and throat.

As with any research study, there may be additional risks that are unknown or unexpected.

5.2 What happens if I get hurt, become sick, or have other problems as a result of this research?

The researchers have taken steps to minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers listed in Section 10 about any injuries, side effects, or other problems that you have during this study. You should also tell your regular doctors.

By signing this form, you do not give up your right to seek payment if you are harmed as a result of being in this study.

5.3 If I take part in this study, can I also participate in other studies?

Being in more than one research study at the same time, or even at different times, may increase the risks to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers involved in each study.

5.4 How could I benefit if I take part in this study? How could others benefit?

You may not receive any personal benefits from being in this study. However, there is a chance that the boost may improve tumor control and increase the length of disease-free survival.

5.5 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?

Yes, the researchers will tell you if they learn of important new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

6. OTHER OPTIONS

6.1 If I decide not to take part in this study, what other options do I have?

If you decide not to participate, you will be treated with the best standard therapy, according to the clinical judgment of your physicians. Other treatments available for your condition include:

- Radiation therapy with concurrent chemotherapy over 7 weeks
- Taking part in another study of an investigational agent (such as surgical removal of your tumor)
- Getting comfort care, also known as palliative care. This type of care helps reduce pain, tiredness, appetite problem and other problems caused by cancer. It does not treat the cancer

7. ENDING THE STUDY

7.1 If I want to stop participating in the study, what should I do?

You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You will not lose any benefits to which you may otherwise be entitled. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please tell one of the persons listed in Section 10 "Contact Information" (below).

7.2 Could there be any harm to me if I decide to leave the study before it is finished?

If you decide to leave the study early, please notify someone on the study team. They will instruct you on how to stop the study safely and you will be advised whether any additional test may need to be done for your safety.

7.3 Could the researchers take me out of the study even if I want to continue to participate?

Yes. There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- ✓ The researcher believes that it is not in your best interest to stay in the study.
- ✓ You become ineligible to participate.
- ✓ Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- ✓ You do not follow instructions from the researchers.
- ✓ The study is suspended or canceled.

8. FINANCIAL INFORMATION

8.1 Who will pay for the costs of the study? Will I or my health plan be billed for any costs of the study?

The study will pay for research-related items or services that are provided only because you are in the study. If you are not sure what these are, see Section 4.1 above or ask the researchers for a list. If you get a bill you think is wrong, call the researchers' number listed in section 10.1.

You or your health plan will pay for all the things you would have paid for even if you were not in the study, like:

- Carboplatin and paclitaxel
- Health care given during the study as part of your regular care
- Items or services needed to give you the carboplatin and paclitaxel and/or radiation therapy
- Monitoring for side effects or other problems
- Deductibles or co-pays for these items or services.
- Treatment complications

If you do not have a health plan, or if you think your health plan may not cover these costs during the study, please talk to the researchers listed in Section 10 below or call your health plan's medical reviewer.

The study team has given you instructions about this research study. It is important that you follow these instructions carefully. If you get sick, have a medical complication, or are injured as a result of your being in the

study, call Dr. Mierzwa, at (734) 845-3914 or at (734) 936-4000 (Hospital Operator – 24-hour paging). The doctor will either treat you or send you to another doctor for treatment.

If you are injured or in the event of a medical emergency, dial 911 or visit your nearest Emergency Room. If you believe the study has made you sick or caused you injury, contact one of the people listed in section 10 of this document (Contact Information). If taking part in the study makes you sick or causes you injury, you will have to arrange for treatment on your own, as the study will not provide medical treatment or provide any compensation to you. You or your insurance provider will be billed for all costs of treatment for sickness or injury caused by the study. It is possible that your insurance will not cover these costs.

By signing this form, you do not give up your right to seek payment if you are harmed as a result of being in this study.

8.2 Will I be paid or given anything for taking part in this study?
You will not be paid for taking part in this research.

8.3 Who could profit or financially benefit from the study results?
Information obtained from this study may help the University of Michigan learn more about the causes, risks, treatments, or how to prevent this and other health problems. The University of Michigan, or physicians at the university could profit financially from this information.

Research can lead to new discoveries, such as new tests, drugs, or devices. Researchers, their organizations, and other entities, including companies, may potentially benefit from the use of the data or discoveries. You will not have rights to these discoveries or any proceeds from them.

9. CONFIDENTIALITY OF SUBJECT RECORDS AND AUTHORIZATION TO RELEASE YOUR PROTECTED HEALTH INFORMATION

The information below describes how your privacy and the confidentiality of your research records will be protected in this study.

9.1 How will the researchers protect my privacy?
The University of Michigan has rules to protect information about you. Federal and state laws also protect your privacy. Upon enrolling in this study, you will be assigned a unique identification number. All records related to the study will use this identification number instead of your name or other personally identifying information whenever possible. We will take measures to protect the privacy and security of all your personal information, but we cannot guarantee complete confidentiality of study data.

Medical information created by this research study may become part of your hospital medical record and may be forwarded to your primary doctor. Information that does not become part of your medical record will be stored in your study file.

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 study treatment or payment for your study treatment, but you may access this information only after the study is completed. To request this information, please contact the researchers listed in Section 10 “Contact Information” (below).

Genetic Risks:

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

information. This law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Under this law:

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

GINA does not apply to the following groups, however these groups have policies in place that provide similar protections against discrimination:

- Members of the US Military receiving care through Tricare
- Veterans receiving care through the Veteran's Administration (VA)
- The Indian Health Service
- Federal employees receiving care through the Federal Employees Health Benefits Plans

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.

9.2 What information about me could be seen by the researchers or by other people? Why? Who might see it?
Signing this form gives the researchers your permission to obtain, use, and share information about you for this study, and is required in order for you to take part in the study. Information about you may be obtained from any hospital, doctor, and other health care provider involved in your care, including:

- Hospital/doctor's office records, including test results (X-rays, blood tests, urine tests, etc.)
- Mental health care records (except psychotherapy notes not kept with your medical records)
- Alcohol/substance abuse treatment records
- HIV/AIDS status
- Sexually transmitted disease or other communicable disease status
- Health plan/health insurance records
- All records relating to your condition, the treatment you have received, and your response to the treatment
- Billing information
- Demographic information
- Personal information

There are many reasons why information about you may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.
- The researchers may need the information to check your test results or look for side effects.
- University of Michigan, Food and Drug Administration (FDA), and/or other government officials, auditors, and/or the IRB may need the information to make sure that the study is done in a safe and proper manner.
- Pfizer or safety monitors or committees may need the information to:
    - Make sure the study is done safely and properly
    - Learn more about side effects
    - Analyze the results of the study

- Insurance companies or other organizations may need the information in order to pay your medical bills or other costs of your participation in the study.
- The researchers may need to use the information to create a databank of information about your condition or its treatment.
- Information about your study participation may be included in your regular University of Michigan medical record.
- Federal or State law may require the study team to give information to government agencies. For example, to prevent harm to you or others, or for public health reasons.

The results of this study could be published in an article, but would not include any information that would let others know who you are.

9.3 What happens to information about me after the study is over or if I cancel my permission?
As a rule, the researchers will not continue to use or disclose information about you, but will keep it secure until it is destroyed. Sometimes, it may be necessary for information about you to continue to be used or disclosed, even after you have canceled your permission or the study is over.

Examples of reasons for this include:

- To avoid losing study results that have already included your information
- To provide limited information for research, education, or other activities (This information would not include your name, social security number, or anything else that could let others know who you are.)
- To help the University of Michigan and government officials make sure that the study was conducted properly

As long as your information is kept within the University of Michigan Health System, it is protected by the Health System's privacy policies. For more information about these policies, ask for a copy of the University of Michigan "Notice of Privacy Practices". This information is also available on the web at http://www.uofmhealth.org/patient+and+visitor+guide/hipaa. Note that once your information has been shared with others as described under Question 9.2, it may no longer be protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA).

9.4 When does my permission expire?
Your permission expires at the end of the study, unless you cancel it sooner. You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below).

10. CONTACT INFORMATION

10.1 Who can I contact about this study?
Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Talk about study-related costs to you or your health plan
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator:	Michelle Mierzwa, DM
Mailing Address:	1500 E. Medical Center Drive Ann Arbor, MI 48109
Telephone:	(734) 845-3914

Emergency Contact: (734) 936-4000 (Hospital Operator – 24-hour paging)

You may also express a concern about a study by contacting the Institutional Review Board listed below.

University of Michigan Medical School Institutional Review Board (IRBMED)
2800 Plymouth Road
Building 520, Room 3214
Ann Arbor, MI 48109-2800
Telephone: 734-763-4768 (For International Studies: US Country Code: 001)
Fax: 734-763-1234
e-mail: irbmed@umich.edu

If you are concerned about a possible violation of your privacy or concerned about a study you may contact the University of Michigan Health System Compliance Help Line at 1-866-990-0111.
When you call or write about a concern, please provide as much information as possible, including the name of the researcher, the IRBMED number (at the top of this form), and details about the problem. This will help University officials to look into your concern. When reporting a concern, you do not have to give your name unless you want to.

11. RECORD OF INFORMATION PROVIDED

11.1 What documents will be given to me?
You will receive a copy of the signed and dated informed consent

Your signature in the next section means that you have received copies of all of the following documents:
This "Consent to be Part of a Research Study" document. (*Note: In addition to the copy you receive,*

- *copies of this document will be stored in a separate confidential research file and may be entered into your regular University of Michigan medical record.)"*
- Other (specify):_____

12. SIGNATURES

Consent/Assent to Participate in the Research Study

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with _____. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

Consent/Assent to Collect and Store OPTIONAL Research Samples for Unspecified Future Research
This project involves the option to allow the study team to keep your identifiable specimens/data for use in future research. I understand that it is my choice whether or not to take part in this optional research. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

_____ Yes, I agree to let the study team keep and store my blood and tissue samples for future research.

_____ No, I do not agree to let the study team keep and store my blood and tissue samples for future research.

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

Principal Investigator or Designee

I have provided this participant and/or his/her legally authorized representative(s) with information about this study that I believe to be accurate and complete. The participant and/or his/her legally authorized representative(s) indicated that he or she understands the nature of the study, including risks and benefits of participating.

Print Legal Name: _____

Title: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

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PERSONAL CENSUS FORM

Name _____ Date _____

The National Cancer Institute requires that The University of Michigan Comprehensive Cancer Center report race and ethnicity information about people who participate in clinical research to ensure that all populations are offered the opportunity to participate.

☐ Check here if you do not wish to provide some or all of the information below.

1. What race do you consider yourself to be? (Please select *one or more*)
   - ☐ American Indian/Alaska Native[a]
   - ☐ Asian[b]
   - ☐ Black or African American[c]
   - ☐ Native Hawaiian or Other Pacific Islander[d]
   - ☐ White[e]
   - ☐ More than one race[f]

2. Do you consider yourself to be Hispanic[g]? ☐ Yes ☐ No

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[a] American Indian or Alaska Native- A person having origins in any of the original peoples of North, Central, or South America, and who maintains tribal affiliation or community attachment.

[b] Asian- A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent, including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand and Vietnam.

[c] Black or African American- A person having origins in any of the black racial groups of Africa. (Terms such as “Haitian” or “Negro” are sometimes used in addition to “Black” or “African American.”)

[d] Native Hawaiian or Other Pacific Islander- A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.

[e] White- A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.

[f] More than one race- (It is preferred that this be selected in addition to the selection of the specific races listed above, but this may also be solely selected.)

[g] Hispanic or Latino- A person of Mexican, Puerto Rican, Cuban, Central or South American, or other Spanish culture or origin, regardless of race. The term “Spanish origin” is sometimes used in addition to “Hispanic” or “Latino.”