CONSENT FOR CANCER RESEARCH

Project Title: A Phase II Trial of modified FOLFOX-6 Induction Chemotherapy Followed by Esophagectomy and Post-operative Response Based Concurrent Chemoradiotherapy in Patients with Locoregionally Advanced Adenocarcinoma of the Esophagus, Gastro-esophageal Junction, and Gastric Cardia.

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Cleveland Clinic Study Coordinator: Denise Ives RN, (216) 444-0192

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, main, Cleveland Clinic Cancer Centers, Sandusky and Wooster Milltown Specialty and Surgery Center.

1. Introduction

We are asking you to participate in a research study. The purpose of this document is to summarize your discussion with the research team and provide you with written information to help you decide whether you want to participate in research. Your decision is completely voluntary.

Your treating doctor may also be an investigator on this research study. If so, your doctor will have an interest in both your welfare and in the research study. You are not required to take part in this research study offered by your doctor. You may ask for a second opinion from another doctor who is not linked to the study. If you choose not to be in this study, the quality of your regular medical care will not be affected.

Please ask any questions you may have about the study or this consent form before signing it. Please take your time to make your decision. You will be given a copy of this form to keep.

One or more of the investigators conducting the study may serve as consultants for the company that makes products used in this study. These financial interests are within permissible limits established by the local institutional Conflicts of Interest Policy. If you have any questions regarding conflicts of interest, please ask your study doctor or call the Cleveland Clinic Institutional Review Board at (216) 444-2924.

2. Purpose

You are being asked to participate in this study because you have an esophageal cancer for which surgical therapy is planned. We know that the addition of chemotherapy and radiation to surgery can improve the results of treatment compared to surgery alone. More specifically, several clinical trials have demonstrated that the administration of chemotherapy before surgery improves outcomes for patients with esophageal cancer. Another large study has demonstrated that the simultaneous administration of chemotherapy and radiation therapy after surgery also

improves outcomes for patients with this disease. Both treatment approaches are considered standard therapy today.

In a prior study at our institution, we combined these two treatment strategies. We tested the safety and efficacy of pre-operative chemotherapy followed by surgery and then chemotherapy and radiation. We demonstrated that this sequence of treatments could be given safely. The results of this study compared favorably with data from other clinical trials as well.

However, we found that patients who did not have a pathologic response (evidence of dead tumor cells) in the surgical specimen (the tumor and portions of the esophagus and stomach removed by surgery) after pre-operative chemotherapy had poor outcomes. In contrast, patients with a strong pathologic response (lots of dead tumor cells) after receiving pre-operative chemotherapy did very well.

The purpose of this study is to determine if we can improve the outcomes of patients who fail to respond to pre-operative therapy and would otherwise be expected to do poorly. In this study, patients who do not obtain a favorable pathologic response to pre-operative chemotherapy will receive a different chemotherapy regimen with radiation after surgery. It is our hope that changing the chemotherapy regimen will help these patients. For patients that have responded to chemotherapy and thereby have obtained a pathologic response, we will continue the same chemotherapy regimen after surgery with radiation.

More specifically, patients will receive pre-operative chemotherapy with a regimen called FOLFOX, which uses the medications 5-fluorouracil, oxaliplatin and leucovorin. Patients who have a good pathologic response to this regimen will receive FOLFOX with radiation after surgery. Patients who did not respond to FOLFOX will alternatively receive the chemotherapy drugs carboplatin and paclitaxel during radiation therapy.

This study is also evaluating the effectiveness of the FOLFOX chemotherapy regimen when given before surgery for esophageal cancer. This regimen is commonly used to treat patients with colon cancer after surgery. It is also very effective in treating patients with spread colon cancer, rectal cancer, and gastroesophageal cancer. Similar chemotherapies have been used to treat patients with esophagus cancer before surgery. We anticipate the FOLFOX regimen will be as effective as these other regimens with less side effects.

There are no experimental chemotherapy drugs, surgical devices, or radiation techniques in this study. We anticipate approximately 66 patients will take part in this research study. This study is available at Cleveland Clinic, main, Cleveland Clinic Cancer Centers, Sandusky and Wooster Milltown Specialty and Surgery

3. Study Procedures

Your participation in this study will require several visits for laboratory studies, imaging investigations, procedures, physician evaluations, chemotherapy, radiotherapy, and surgery as outlined below. The total duration of therapy will last approximately 7 months, from the time of initial screening procedures until the last dose of radiotherapy. After the completion of the study therapy, you will be followed in the clinic on a periodic basis (see below) for at least 5 years.

Please note, the current standard therapies for this disease often require a similar number of visits.

Screening:

Before you begin the study, a number of tests will need to be done to determine if you are eligible for this trial and if you are well enough to receive these treatments. These studies will be obtained within 42 days (6 weeks) of starting therapy.

- A medical history.
- A physical examination.
- Performance status evaluation: An assessment by your doctor of your activity level.
- Upper endoscopy with ultrasound and biopsy: A procedure to look into your esophagus with an endoscope and measure with an ultrasound the size of your tumor. At the same time, the physician will obtain a small piece of the tumor for further testing.
- PET/CT: An imaging procedure to allow your doctor to know where the cancer is in your body.
- Lung function tests: Breathing tests that let your doctor know if you are well enough to receive the study treatment.
- A heart stress test.
- Blood tests: Laboratory studies that let us know how your liver and kidneys are working and to make sure you have normal blood counts.
- Pregnancy test in women who are able to become pregnant.
- Special studies on your tumor: As part of this study, we will perform special tests on the biopsy obtained during the endoscopic ultrasound.

Infuse-a-Port (port) and computerized ambulatory drug delivery pump (CADD):

The chemotherapy used in this study requires the placement of a device called an Infuse-a-Port. This is a small device placed under the skin of the chest near the collarbone. Attached to this device is a small catheter which is inserted into the vein under the collarbone. A port is required for the administration of chemotherapy in this study because one of the study drugs, 5-fluorouracil, is given over the course of 2 days. This is chemotherapy that you will receive at home. Therefore, a safe and reliable method of administration is required. A port is basically a very good intravenous catheter that can be left in place for an extended period of time. It would not be possible to send you home with chemotherapy being infused through a small IV placed in your forearm. This is why port is required.

Port placement is generally done by radiologists. This is an outpatient procedure for which you receive slight sedation and local anesthesia. The procedure generally takes half an hour. When your treatment is completed we anticipate removal of this port, again, with a simple outpatient procedure under local anesthesia.

The CADD is a device which holds the chemotherapy and automatically infuses it into the port while you are at home. The CADD is approximately the size of your wallet. It can be worn attached to your belt or as a shoulder bag while you're receiving chemotherapy. It is attached to the port by tubing and a small needle which is used to access the port. The needle and tubing is

secured in place by our nursing staff. You will not need to manage this device at home. The CADD will automatically administer chemotherapy.

What happens if I have problems with my CADD during treatment? Support is available 24 hours per day and is provided for all patients using a CADD at the Cleveland Clinic by INFU System. The support phone number is (800) 315-3287. The website is www.infusystem.com.

Can I shower or bath with my CADD? The CADD cannot get wet. We recommend taking "sponge baths" while you are receiving chemotherapy with the CADD through the port. A "sponge bath" is a bath in a small amount of water and a damp towel is used for cleaning purposes.

Pre-operative Chemotherapy:

Once all of the screening studies have been performed and you have signed this informed consent document, you will be able to begin the study treatment. In the first part of this study, all patients are scheduled to receive 4 rounds of chemotherapy with the FOLFOX regimen which is given every 2 weeks. Prior to chemotherapy a nurse will stick a needle in your port. This is referred to as accessing the port. Blood samples will be obtained through the port to make sure that your blood counts are appropriate for chemotherapy. You will also receive intravenous medicines through the port to prevent nausea. Once you receive these medicines and we are sure that your blood counts are acceptable for treatment, you will receive chemotherapy.

The FOLFOX regimen consists of 2 chemotherapy drugs: Oxaliplatin and 5-Fluorouracil. Oxaliplatin is given over 2 hours through the port. 5-fluorouracil is also administered intravenously through the port. You will receive a small dose of 5-fluorouracil over the course of a few minutes in our clinic. The nursing staff then attaches the CADD to your port and a larger dose of 5-fluorouracil will then administered over the course of 46 hours. Two days after you initially received each dose of chemotherapy, you will be brought back to the Cleveland clinic Taussig Cancer Center where the CADD will be removed and the needle will be taken out of your port. Removing the needle from the port is referred to as being de-accessed.

Restaging after pre-operative chemotherapy:

Approximately 3-4 weeks after you complete chemotherapy, you will be evaluated with a CT scan of the chest, abdomen, and pelvis. You will also have a repeat upper endoscopy with an ultrasound study to evaluate the size and condition of your esophageal cancer after treatment. Blood tests will also be obtained to ensure adequate recovery of your bone marrow and appropriate kidney and liver function. You will also have blood work to determine whether or not you have circulating tumor cells, and to quantify these cells if present. You will see your doctor to review these studies prior to undergoing surgery

Surgery:

Surgery is expected to take place 4-5 weeks after completion of chemotherapy. The surgery, and all post-surgical care, is performed in a standard fashion. There are no experimental components of surgery. The operation can be performed using various incisions. Most of the esophagus and

a portion of the stomach are usually removed. The remainder of the stomach is then used to reconstruct the esophagus, being brought into the chest and connected with the remaining esophagus in the neck. In some circumstances, the entire stomach is removed as well. In this setting, small intestine is often used to reconstruct the esophagus. In rare instances, the esophagus cannot be immediately reconstructed. In this situation, a restorative operation is performed at a later date, potentially 6 to 12 months from the initial surgery. The choice of surgical incision, extent of the operation, and type of reconstruction performed are at the discretion of your surgeon.

The hospital stay is approximately 10-14 days. All patients have a feeding tube placed at the time of surgery which travels through the abdominal wall and ends in a section of small bowel referred to as the jejunum. This tube is referred to as a jejunostomy tube. You will initially receive all nutrition through this tube. The tube remains in until all chemotherapy and radiation is complete and you have sufficiently recovered. This is expected to be 4 to 5 months from the time of surgery.

Post-operative evaluation:

You will be reevaluated by your doctor approximately 4 weeks after surgery. At this visit, blood work will be obtained and you doctor will review the results of your surgical pathology. Surgical pathology refers to the microscopic description of your tumor. We will determine if all the tumor has been removed, the size of the tumor, and whether or not it has traveled to any lymph nodes. We also will evaluate if chemotherapy killed the cancer cells and to what degree. Special tests will be performed on your specimen as part of this study. These tests include the Ki67 test, which evaluates how many tumor cells are growing, and the HER2 test, which evaluates for the presence of a gene / protein thought to be important for esophageal cancer growth.

At this visit your doctor will determine your post-operative chemotherapy regimen based on the amount of living cancer cells demonstrated in your surgical pathology.

Post-operative chemoradiation:

Between 6-12 weeks after surgery you will be treated with chemotherapy and radiation. The purpose of this treatment is to potentially eradicate any tumor cells around the site were the tumor was located which were not removed by surgery. Chemotherapy makes the radiation work more effectively, and also continues to treat any microscopic tumor cells that spread to distant organs prior to surgery.

Radiation therapy is administered once a day, usually Monday through Friday. The total duration of treatment is approximately 5 and 1/2 weeks. Radiation is not typically administered on weekends. The treatment lasts no longer than 20 minutes. Radiation consists of high energy beams which are not visible to the naked eye. Careful planning is required to minimize radiation exposure to the lungs, heart, spinal cord, and other vital structures.

Chemotherapy will be given concurrently with radiation. The chemotherapy you receive will depend on the analysis of your surgical pathology. Patients who are found to have low residual viable tumor cells (lots of dead cancer cells) will receive FOLFOX chemotherapy again during radiation. FOLFOX will be administered as outlined above. Patients who did not appear to

benefit from preoperative FOLFOX chemotherapy, and therefore have high residual viable tumor cells (mostly living cancer cells), will receive the alternative chemotherapy regimen, carboplatin and paclitaxel. This chemotherapy regimen is administered through an IV (your port) once a week during radiation treatment. Similar to FOLFOX chemotherapy, you will have blood work obtained through your port prior to treatment. This will be done to assure that your blood counts are appropriate for chemotherapy that day. You will then receive medicines to prevent nausea. Once we know that your blood work is acceptable and you have received the preventative medicines, chemotherapy will be administered. This takes approximately 3 hours. Unlike FOLFOX chemotherapy, there is no infusion of chemotherapy received at home with carboplatin and paclitaxel.

Follow-up:

Once you have completed this treatment regimen, you will be seen periodically by your physician. At those visits, any blood work or imaging investigations that are performed are done so at the discretion of your physician and will be obtained based on your symptoms. You will be seen every 3 months for the first 2 years from the completion of treatment. After that, you will be evaluated every 4-6 months for a total of 5 years from the completion of treatment. After 5 years annual follow-up evaluation is recommended.

These visits will last approximately 20-30 minutes. Your doctor will ask you how you are feeling, perform a physical examination, and periodically obtain x-rays, scans or blood work according to the routine management used in patients with this disease.

Discontinuation of study treatment:

You may withdraw from this study at any time and for any reason. Your doctor may also decide to remove you from the study if he/she feels it is in your best interest. Patients who experience certain toxicities will be removed from the study as well. Patients who are removed from the study will continue to be followed, unless you specifically request otherwise.

4. Risks

Participation in this study involves physical risk, including death. However, there are no experimental therapies employed in this treatment protocol. Therefore, all risks attributed to participation in this trial are similar to what would be expected with standard care of this disease. However, we cannot anticipate all risks or potential side effects. Your condition may worsen on this investigational treatment regimen.

Chemotherapy:

Oxaliplatin

Common (occurs 50% of the time or greater in subjects)

- Low white blood cell count (cells that fight infection),
- Red blood cell count (anemia)
- Platelets (blood cells which help stop bleeding)

- Fatigue
- Loss of appetite
- Altered taste
- Nausea
- Peripheral neuropathy: a condition in which you may experience pain or numbness in the tips of your fingers or toes. This neuropathy may be briefly exacerbated by cold exposure (putting your hand in the refrigerator, for example).

Less common (occurs 10-50% of the time in subjects)

- Liver damage usually detected by blood work
- Ulceration of the lips and mouth (referred to as stomatitis and mucositis, respectively)
- Diarrhea
- Constipation
- Abdominal pain
- Headache
- Insomnia (trouble sleeping)

Rare (occurs less than 10% of the time in subjects)

- Serious infections related to a low white blood cell count which requires hospitalization.
- Allergic reactions to the chemotherapy, which can result in anaphylactic shock (low blood pressure, trouble breathing, tongue swelling, rash)
- Lung damage
- Severe liver damage
- Electrolyte abnormalities (low blood potassium, magnesium, calcium)
- Hair loss.
- Laryngopharyngeal dyesthesia (LPD): a condition experienced during or shortly after the infusion of oxaliplatin which may produce jaw pain or discomfort as well as a feeling of breathlessness. It has been described as feeling as if the "throat is closing," however, this is a sensation with no physical harm. The throat is not closing and your breathing is not impaired. LPD must be distinguished from allergic reactions.

5-Fluorouracil

Common (occurs 50% of the time or greater in subjects)

- Fatigue
- Loss of appetite
- Altered taste
- Low blood counts (white cells, red cells, and platelets) as described above (see oxaliplatin common toxicity).

Less common (occurs 10-50% of the time in subjects)

- Ulcerations of the lips and mouth (stomatitis, mucositis)
- Nausea
- Vomiting
- Diarrhea
- Abdominal pain
- Hand foot syndrome (HFS): a condition in which you may experience pain and redness of the palms and soles. This is often accompanied by dryness and cracking of the skin. Nail changes, skin changes (darkening) and photosensitivity (increased skin sensitivity to sunlight). Liver damage usually detected by blood work.

Rare (occurs less than 10% of the time in subjects)

- Hair loss
- Excessive tearing
- Visual changes
- Photophobia (headache or eye pain with exposure to ambient or bright light).
- Confusion and loss of balance
- Severe allergic reactions (including anaphylactic shock, please refer to oxaliplatin rare toxicity above).
- Chest pain (angina) and heart attack
- Serious infections related to a low white blood cell count which requires hospitalization.

Carboplatin

Common (occurs 50% of the time or greater in subjects)

- Fatigue
- Loss of appetite
- Altered taste
- Low blood counts (white cells, red cells, and platelets) as described above (see oxaliplatin common toxicity).

Less common (occurs 10-50% of the time in subjects)

- Liver damage usually detected by blood work
- Electrolyte abnormalities (low sodium, low potassium, low magnesium, low calcium).
- Abdominal pain
- Nausea
- Vomiting
- Diarrhea

Rare (occurs less than 10% of the time in subjects)

- Kidney damage
- Hair loss
- Allergic reactions including anaphylactic shock (see oxaliplatin rare toxicity above)
- Ulcerations of the lips and mouth (stomatitis and mucositis, respectively).
- Peripheral neuropathy (numbness/tingling and/or pain of the fingers and toes)
- Loss of balance, confusion, and visual changes
- Serious infections related to a low white blood cell count that requires hospitalization.

Paclitaxel

Common (occurs 50% of the time or greater in subjects)

- Hair loss
- Fatigue
- Loss of appetite

- Altered taste
- Low blood counts (white cells, red cells, and platelets) as described above (see oxaliplatin common toxicity).

Less common (occurs 10-50% of the time in subjects)

- Liver damage usually detected by blood work
- Ulcerations of the lips and mouth (stomatitis and mucositis)
- Muscle and joint pain
- Nausea, vomiting, and diarrhea.
- Peripheral neuropathy (numbness/tingling and/or pain of the fingers and toes).

Rare (occurs less than 10% of the time in subjects)

- Allergic reactions including anaphylactic shock (see oxaliplatin rare toxicity above)
- Abnormal heart beat / rhythm
- Lung damage, liver damage
- Serious infections related to low white blood cell count which requires hospitalization.

Radiation: A separate and more inclusive consent procedure will be provided by radiation oncology. This serves as an overview.

Fatigue and loss of appetite. Esophagitis/gastritis/enteritis: Inflammation of the lining of the esophagus, stomach, or intestines as a direct consequence of radiation. This may cause chest or upper abdominal discomfort or pain. Nausea and vomiting. Low blood counts (white cells, red cells, and platelets. See oxaliplatin common toxicity above). A sunburn reaction on the skin of the chest or upper abdomen. Bleeding, perforation (a small hole in the esophagus, stomach, or intestine). Inflammation of the lungs or lining of heart.

Surgery: A separate and more inclusive consent procedure will be provided by your surgeon. This serves as an overview.

Lung complications are common and include infection (pneumonia), the accumulation of fluid around the lungs (referred to a pleural effusion), areas of collapsed lung (referred to as atelectasis) and lung damage. Heart problems include heart attacks, heart failure, and abnormal heart rhythms. Some patients also develop a fluid accumulation around the heart (referred to as pericardial effusion). Occasionally the nerve that controls the vocal cords is damaged. This may result in a hoarse voice and trouble swallowing food. Sometimes the connection created by the surgeon between the remaining esophagus and the stomach or intestines (new esophagus) will form a small whole and leak. Later side effects of surgery include trouble swallowing, heartburn, and the inability to eat large meals. Certain foods may also cause abdominal bloating,

pain, or diarrhea. This is referred to as dumping syndrome. While rare, surgery may result in death.

Reproductive health/sexual activity:

Chemotherapy may cause birth defects in the fetus, especially when administered to pregnant women in the first trimester. For that reason, if you are pregnant, or are planning to become pregnant, you may not participate in this study. Before you enter the study, female patients of childbearing potential will have a pregnancy test. If you are women of childbearing potential, you may participate only if you are using a reliable method of birth control. The study doctor will discuss appropriate birth control measures with you. If you suspect that you are pregnant during the study, you must notify the study doctor immediately. In addition, if you are nursing a child, you may not participate in this study.

The treatment used in this study could also affect sperm and could potentially harm a child that is conceived while on this study. If you are sexually active male and your partner is a female of child bearing potential, you must agree to use a medically acceptable form of birth control in order to be in this study. Medically acceptable contraceptives include: (1) surgical sterilization, or (2) a condom used with a spermicide.

5. Benefits

There is no guarantee that you will benefit from participation in this trial. The appropriate management of patients who do not appear to have benefited from preoperative therapy is unclear. These patients generally have worse outcomes. This study is investigating the use of a different chemotherapy regimen for patients who fail to respond adequately to pre-operative treatment. Therefore, we hope to improve the outcomes in this group of patients.

Your participation in this study may also aid our understanding of the management of locally advanced esophagus cancer. This includes our understanding of the effectiveness of the FOLFOX chemotherapy regimen in the preoperative setting, the role of various biomarkers (circulating tumor cells, Ki-67, HER-2) in predicting the response to treatment and therapy outcomes, and the efficacy of the overall treatment design.

6. Alternatives to Participation

Because of the nature of this research, the only alternative is to not participate in this study.

What are my options if I choose not to participate?

Standard therapy for this disease entails other combinations of chemotherapy and radiation administered before or after surgery. The two most commonly utilized treatment schedules are as follows:

1) Chemotherapy and radiation administered at the same time before surgery

2) Chemotherapy administered before and after surgery without radiation

All components of this investigational protocol are commercially available. There are no investigational drugs included in our study.

Do I have other options aside from those listed above?

Other options include participating in a different clinical trial at a separate institution.

You may also decide to receive only therapies which will provide a symptomatic benefit but not offer a chance for cure. This would include a short course of radiation to the esophagus or placement of an esophageal stent to help improve your swallowing.

Is surgery necessary?

We believe that the best management of this disease requires surgery. However, for patients who are either medically unfit for surgery or decline the operation, we administer chemotherapy and radiation at the same time over the course of 5-6 weeks. This treatment approach can infrequently eliminate the disease. In the remainder of patients, it often prevents the tumor from growing or spreading for approximately 1- 2 years, on average.

7. Costs and Compensation

All of the treatments employed in this study are approved by the FDA. All of the treatments are commercially available. Therefore, you or your insurance company will be responsible for the cost of care. The study will pay for any exploratory tests or procedures. This includes special testing (Ki67 and HER2) on your biopsy / pathology specimens. You will not be reimbursed for your participation in this study.

For more information on clinical trial and insurance coverage, you can visit the National Cancer Institute's (NCI) website at
http://cancer.gov/clinicaltrials/understanding/insurance-coverage
You can print a copy of the 'Clinical Trials and Insurance Coverage' information from this website. Another way to get information is to call 1-800-4-CANCER (1-800-422-6237) and ask NCI for a free copy.

8. Research Related Injury

If you experience physical injury or illness as a result of participating in this research study, medical care is available at the Cleveland Clinic or elsewhere; however, the Cleveland Clinic has no plans to provide free care or compensation for lost wages.

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

9. Privacy and Confidentiality

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 the Cleveland Clinic Principal Investigator, Michael J. McNamara MD, and the research 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:

- Data Safety and Monitoring Boards;
- The Food and Drug Administration;
- The Department of Health and Human Services;
- The National Cancer Institute (NCI); their Institutional Review Boards;

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: Michael J. McNamara, M.D., Cleveland Clinic, Taussig Cancer Institute, Solid Tumor Oncology, 9500 Euclid Avenue, R35, Cleveland Ohio, 44195 / (216) 444-5110.

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.

10. 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.

Termination of Participation

Your participation in this study may be discontinued by your doctor without your consent. Reasons to discontinue participation in this study would include:

- Your doctor feels it is in your best interest
- You develop troublesome side effects from the study therapy
- You develop a medical condition during the study which would make further therapy dangerous

11. Questions About The Research

If you have any questions, you can ask the Principal Investigator and/or research staff.

Michael J. McNamara, M.D.
Phone: (216) 444-5110

Emergency and After-hours Contact Information

If you are a Cleveland Clinic 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 have questions about your rights as a research subject, you may contact the Institutional Review Board (IRB) at Cleveland Clinic IRB 216-444-2924.

Where Can I Get More Information?

You may call the National Cancer Institute's Cancer Information Services at:

1-800-4-CANCER (1-800-422-6237) or TTY: 1-800-332-8615

You may also visit the NCI website 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, 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