

MARQUETTE GENERAL HEALTH SYSTEM
Regional Medical Center

CONSENT TO PARTICIPATE IN AN INVESTIGATIONAL STUDY

TITLE: RTOG 0617 A RANDOMIZED PHASE III COMPARISON OF STANDARD- DOSE (60 Gy) VERSUS HIGH-DOSE (74 Gy) CONFORMAL RADIOTHERAPY WITH CONCURRENT AND CONSOLIDATION CARBOPLATIN/PACLITAXEL IN PATIENTS WITH STAGE IIIA/IIIB NON-SMALL CELL LUNG CANCER

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This is a clinical trial, a type of research study. Your study doctor (and/or people on your doctor's team who are familiar with this study) will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask your study doctor for more explanation.

You are being asked to take part in this study because you have lung cancer that has spread to regional lymph nodes and are not a candidate for surgery.

Why is this study being done?

The purpose of this study is to...

Compare the effects, good and/or bad, of high-dose radiation therapy with standard dose radiation therapy on you and your Stage III non-small cell lung cancer to find out which is better. In this study, you will get either the high-dose or the standard-dose radiation therapy. You will not get both. Everyone will get the chemotherapy with the same drug combination and schedule, consisting of paclitaxel and carboplatin.

How many people will take part in the study?

About 512 people will take part in this study. About half of the patients will receive high-dose radiation therapy and about half will receive standard dose radiation therapy.

What will happen if I take part in this research study?

Before you begin the study ...

You will need to have the following exams, tests or procedures to find out if you can be in the study. These exams, tests or procedures are part of regular cancer care and may

be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- History and physical examination
- A biopsy of your tumor proving that you have cancer
- CT scan of the chest and upper abdomen
- MRI scan of the brain (or CT if the MRI cannot be performed for medical reasons)
- Body FDG-PET or PET-CT scan or bone scan
- Routine blood tests
- Pulmonary function studies

During the study ...

If the exams, tests and procedures show that you can be in the study, and you choose to take part, then you will need the following tests and procedures. They are part of regular cancer care.

- Physical exam – at 3 weeks, 6 weeks, 3 months, and then every 3 months for the first year, every 4 months for the second year, every 6 months for years 3-5, and yearly thereafter.
- Routine blood tests – weekly at 3 weeks and 6 weeks, otherwise as ordered by your doctor
- CT imaging to follow the cancer – at 3 months, 6 months, and then every 3 months for the first year, every 4 months for the second year, every 6 months for years 3-5, and yearly thereafter.
- Pulmonary function testing at 6 and 12 months after completing therapy.
- Additional x-rays, bone scan, and/or PET scan will be done if indicated by your doctor.

You will be "randomized" into one of the study groups described below. Randomization means that you are put into a group by chance. A computer program will place you in one of the study groups. Neither you nor your study doctor can choose the group you will be in. You will have a 50% chance of being placed in one of two groups.

If you are in group 1 (called "Arm A") ...

You will receive the standard or usual dose of radiation therapy (60 Gray given in 30 treatments). You will receive treatment radiation therapy 5 days per week for about 6 weeks. Chemotherapy consisting of paclitaxel and carboplatin will be given on days 1, 8, 15, 22, 29, 35, and 42 during radiation therapy. You will receive two additional cycles of chemotherapy approximately 4 weeks after completion of the combined chemotherapy and radiation.

If you are in group 2 (called "Arm B")...

You will receive a higher than standard dose of radiation therapy (74 Gray given in 37 treatments). You will receive treatment radiation therapy 5 days per week for 7½ weeks. Chemotherapy consisting of paclitaxel and carboplatin will be given weekly on days 1,

8, 15, 22, 29, 35, and 42 during radiation therapy. You will receive two additional cycles of chemotherapy on days 70 and 91 after completion of the combined chemotherapy and radiation.

Both groups will receive chemotherapy with the same drug combination, dose, and schedule. Paclitaxel and carboplatin are given by vein before radiation therapy. The paclitaxel takes one hour to be given after you have been pre-medicated with medicines to ease possible side effects. After the paclitaxel, the carboplatin is given over 30 minutes along with drugs used to prevent or reduce upset stomach and vomiting.

When I am finished taking this treatment...

A series of follow up tests will be performed in order to determine the effect of the treatment on your cancer, on your overall health, and on your quality of life.

- You will be scheduled for CT imaging of your cancer every three months for year 1, every 4 months for year 2, every 6 months for years 3-5, and annually thereafter. You will visit with your study doctor after each of these tests is completed. During these visits, the study doctor will interview and examine you and discuss these results with you.
- You will have pulmonary function tests performed after 6 months and 12 months in order to determine your breathing function after treatment compared to before treatment. Each of these is a part of routine care.

How long will I be in the study?

You will receive radiation therapy for either 6 or 7 ½ weeks (depending on which radiation dose you are assigned) along with weekly chemotherapy. After you are finished taking radiation therapy, you will be given 2 additional cycles of chemotherapy. The planned interval between finishing the radiation and starting the additional chemotherapy is one month. This chemotherapy will consist of the same drugs given previously (carboplatin and paclitaxel) except at higher doses, separated by three weeks in between. Therefore, the total time you will receive treatment is approximately 14 weeks or 16½ weeks depending on the treatment arm to which you are assigned. Follow up visits and exams will continue for the rest of your life according to the schedule given above, in order to monitor the status of your cancer.

Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely.

It is important to tell the study doctor if you are thinking about stopping so any risks from the treatment can be evaluated by him/her. Another reason to tell your study doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest; if you do not follow the study rules; or if the study is stopped.

What side effects or risks can I expect from being in the study?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, researchers don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the radiation or chemotherapy. In some cases, side effects can be serious, long lasting, or may never go away. There also is a risk of death from either radiation therapy or chemotherapy.

You should talk to your study doctor about any side effects that you have while taking part in the study.

Risks and side effects related to radiation therapy to the chest include those which are:
Risks and side effects on Arm B may be greater than on Arm A. Specifically, side effects with swallowing, cough, and/or lung damage may be greater on Arm B.

Likely

- Difficulty, pain, or a burning sensation when swallowing, which is temporary
- Fatigue, which is temporary
- Tanning, redness of the skin, and hair loss within the treatment area, which is temporary
- Skin in the treatment area may remain permanently dry, and chest hair may not grow back
- Decrease in blood counts while undergoing treatment that may result in bleeding, and bruising easily
- Cough and some difficulty in breathing due to lung damage

Less Likely

- Narrowing of the esophagus causing difficulty swallowing meals (requiring internal dilation or a feeding tube)

Rare but serious (late)

- Pericarditis – irritation of the heart sac causing a rapid heart rate, chest discomfort, or chest pain
- Myocarditis – irritation of the heart muscle causing shortness of breath, chest pain, or permanent heart muscle damage
- Transverse myelitis – irritation of the spinal cord causing weakness or paralysis
- Bleeding from the airway
- Narrowing of the airway causing shortness of breath
- Death

Risks and side effects associated with Paclitaxel

Likely

- Low pulse
- Low blood pressure
- Loss of hair
- Tingling, numbness, burning pain in hands and feet
- A decrease in white blood cells, which could lead to infection
- A decrease in platelets, which could lead to bleeding
- Skin redness or rash
- Fatigue
- Nausea and/or vomiting
- Mouth sores
- Diarrhea
- Anemia, a lower than normal number of red blood cells
- Swelling of the legs, arms, or feet
- Cardiovascular changes on EKG (test that measures electrical signal of heart)

Less Likely

- Injection site reaction
- Blurred vision
- Skin or nail darkening
- Aches and pains in muscles and joints
- Fever

Rare but serious

- Temporary changes in blood tests measuring liver function
- Abnormal heart rhythms, which could be life threatening
- Severe allergic reactions
- Fever
- Temporary “bright spots” in vision
- Severe rash called “Stevens- Johnson Syndrome” that can cause fever and severe eruptions of blisters which can occur on the skin of the trunk of the body, mouth, eyes, and genitals
- Death

Risks and side effects associated with Carboplatin

Likely

- A decrease in white blood cells, which could lead to infection
- A decrease in platelets, which could lead to bleeding
- Anemia, a lower than normal number of red blood cells
- Nausea and/or vomiting
- Diarrhea
- Fatigue

- Loss of hair
- Temporary changes in blood tests which measure kidney or liver function
- Low sodium in the blood, which could result in bloating and puffiness in the face and fingers, nausea, vomiting, muscle weakness, headache, and disorientation
- Low magnesium in the blood, which could result in increased irritability of the nervous system with spasms of the hands and feet, muscular twitching, and cramps
- Low calcium in the blood, which could result in numbness or tingling around the mouth or in the feet and hands, as well as in muscle spasms in the face, feet, and hands
- Low potassium in the blood, which could result in muscle weakness, cramping, muscle limpness, and/or irregular heartbeat

Less Likely

- Weakness, loss of strength
- Pain
- Mouth sores
- Tingling, numbness, burning pain in hands and feet, which may be persistent or permanent
- Inflammation of the lung, which could lead to cough and shortness of breath

Rare but serious

- Blurred vision
- Hearing loss
- Allergic reactions
- Irregular heartbeats
- Shortness of breath
- Hemolytic-uremic syndrome (HUS), a disorder that results in the destruction of red blood cells and platelets with decreased kidney function
- A risk of developing a second cancer unrelated to the treated lung cancer, which may occur months or years after initial treatment
- Death

Reproductive risks: You should not become pregnant or father a baby while on this study because the drugs in this study can affect an unborn baby. Women should not breastfeed a baby while on this study. It is important you understand that you need to use birth control while on this study. Check with your study doctor about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study. Some of the drugs used in the study may make you unable to have children in the future. Pregnancy testing may be required if you are female and are able to have children.

For more information about risks and side effects, ask your study doctor.

Are there benefits to taking part in the study?

Taking part in this study may or may not make your health better. The advantage to participating in this Phase III study is that multiple experts in lung cancer have participated in

the design, writing or review of this study. The participants that are assigned to the higher dose of radiation therapy may or may not benefit from the extra treatments. We do know that the information from this study will help researchers learn more about whether or not the extra treatment offers any further benefit. This information could help future cancer patients.

What other choices do I have if I do not take part in this study?

Your other choices may include:

- **Getting treatment or care for your cancer without being in a study**
- **Taking part in another study**
- **Getting no treatment**

Talk to your study doctor about your choices before you decide if you will take part in this study.

Will my medical information be kept private?

Data are housed at RTOG Headquarters in a password-protected database. We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The local institutional review board at the center where you are treated
- Auditors and researchers from the RTOG, CALGB, and/or NCCTG that are associated with the study
- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people
- The Cancer Trials Support Unit (CTSU), a research group sponsored by the National Cancer Institute (NCI) to provide greater access to cancer trials

What are the costs of taking part in this study?

You and/or your health plan/ insurance company will need to pay for some or all of the costs of treating your cancer in this study. Some health plans will not pay these costs for people taking part in studies. Phase III studies like this one are generally covered by insurance. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

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

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at <http://cancer.gov/clinicaltrials/understanding/insurance-coverage>. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

What happens if I am injured because I took part in this study?

It is important that you tell your study doctor, Dr. Nelson Adamson, if you feel that you have been injured because of taking part in this study. You can tell the study doctor in person or call him/her at 906-776-5975

You will get medical treatment if you are injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. The study will not pay for medical treatment.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

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

A Data Safety Monitoring Board will be regularly meeting to monitor safety and other data related to this study. The Board members may receive confidential patient information, but they will not receive your name or other information that would allow them to identify you by name.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?

You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor Dr. Nelson Adamson at 906-776-5975.

For questions about your rights while taking part in this study, call the Patient Advocate at 906-225-3433.

Please note: This section of the informed consent form is about additional research that is being done with people who are taking part in the main study. You may take part in this additional research if you want to. You can still be a part of the main study even if you say ‘no’ to taking part in this additional research.

You can say “yes” or “no” to [each of] the following study[ies]. Below, please mark your choice [for each study].

Quality of Life Study

We want to know your view of how your life has been affected by cancer and its treatment. This “Quality of life” study looks at how you are feeling physically and emotionally during your cancer treatment. It also looks at how you are able to carry out your day-to-day activities.

This information will help doctors better understand how patients feel during treatments and what effects the medicines are having. In the future, this information may help patients and doctors as they decide which medicines to use to treat cancer.

You will be asked to fill out two questionnaires at the following five time points in order to assess the impact of this therapy on your quality of life: before treatment, at the end of chemoradiation therapy, at 3 months, 12 months, and at 2 years. There are two questionnaires per time point; one called the FACT-TOI that takes approximately 10 minutes to complete and one called the EQ-5D that takes approximately 5 minutes to complete.

You will also be given a swallowing diary and asked to enter a daily score of your swallowing symptoms (ability to swallow) during the course of chemoradiation and twice more during the follow-up chemotherapy. This will take a few minutes per week. You will be asked to turn in your swallowing diary at the end of the treatment.

If any questions make you feel uncomfortable, you may skip those questions and not give an answer.

If you decide to take part in this quality of life study, you will be asked to fill out the two questionnaires (at the five timepoints above) and the weekly swallowing diary. You may change your mind about completing these forms at any time.

Just like in the main study, we will do our best to make sure that your personal information will be kept private.

Please circle your answer.

I choose to take part in the Quality of Life Study. I agree to fill out the two Quality of Life Questionnaires and the swallowing diary.

YES

NO

Use of Tissue for Research and Collection of Blood and Urine

Consent Form for Use of Tissue for Research

About Using Tissue for Research

You will have had a biopsy to see if you have cancer. Your doctor will remove some tumor tissue to do some tests. The results of these tests will be given to you by your doctor and will be used to plan your care.

We would like to keep some of the tissue that is left over for future research. In addition to the tumor tissue, we would like to collect some blood and urine. You will be asked to provide about 4 teaspoons of blood and about 2 teaspoons of urine at the following time points: before treatment, four weeks after the start of treatment, and at your first follow-up visit after completion of chemoradiotherapy

If you agree, this tissue, blood, and urine will be kept and may be used in research to learn more about cancer and other diseases. Please read the information sheet called "How is Tissue Used for Research" to learn more about tissue research. This information sheet is available to all at the following web site:

<http://www.cancerdiagnosis.nci.nih.gov/specimens/patient.pdf>

The research that may be done with your tissue is not designed specifically to help you. It might help people who have cancer and other diseases in the future.

Reports about research done with your tissue will not be given to you or your doctor. These reports will not be put in your health record. The research will not have an effect on your care.

Things to Think About

The choice to let us keep the left over tissue for future research is up to you. No matter what you decide to do, it will not affect your care or your participation in the main part of the study.

If you decide now that your tissue can be kept for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use your tissue. Then any tissue that remains will no longer be used for research and will be returned to the institution that submitted it and leftover blood and urine will be destroyed.

In the future, people who do research may need to know more about your health. While the doctor/institution may give them reports about your health, it will not give them your name, address, phone number, or any other information that will let the researchers know who you are.

Sometimes tissue is used for genetic research (about diseases that are passed on in families). Even if your tissue is used for this kind of research, the results will not be put in your health records.

Your tissue will be used only for research and will not be sold. The research done with your tissue may help to develop new treatments for cancer in the future.

Benefits

The benefits of research using tissue include learning more about what causes cancer and other diseases, how to prevent them, and how to treat them.

Risks

The greatest risk to you is the release of information from your health records. We will do our best to make sure that your personal information will be kept private. The chance that this information will be given to someone else is very small.

Making Your Choice

Please read each sentence below and think about your choice. After reading each sentence, circle "Yes" or "No". If you have any questions, please talk to your doctor or nurse, or call our research review board at IRB's phone number.

No matter what you decide to do, it will not affect your care.

1. My tissue/blood/urine may be kept for use in research to learn about, prevent, or treat cancer.

Yes No

2. My tissue/blood/urine may be kept for use in research to learn about, prevent or treat other health problems (for example: diabetes, Alzheimer's disease, or heart disease).

Yes No

3. Someone may contact me in the future to ask me to take part in more research.

Yes No

Where can I get more information?

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

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

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.

COSTS AND PAYMENTS:

You understand that the Group, DCHS, and MGHS furnish no funds providing medical treatment for, or financial compensation to, human subjects in the event the investigational therapy results in loss or injury. You will be responsible for the cost of emergency medical treatment provided by this institution and/or by your physician. You are also aware that the ...Group and Marquette General Hospital will not take financial responsibility for non-acute medical problems.

Lab tests (blood), x-rays and other diagnostic tests will be done frequently to check the effects of the investigational therapy. You understand that the costs of your medication and treatment may exceed what your insurance company is willing to pay, and that you will be responsible for payment. In many instances, however, all or a portion of those costs may be reimbursed by your insurance company.

INSTITUTIONAL FUNDING:

Funds are provided from the study sponsor to Marquette General Hospital on a per patient basis to help with the institution's costs of participating in this study.

OTHER OPTIONS:

Comfort care only, where treatments are directed only at reducing symptoms, relieving suffering and maximizing comfort, dignity, and control. In comfort care only, treatment is not directed at curing, slowing or reversing your disease. Please ask any questions you may have and take as much time as you need to make your decision.

CONFIDENTIALITY:

We will keep any information we learn from this study confidential and disclose it only with your permission, except as required by law. By signing this form, however, you allow us to make your records available to the National Cancer Institute, the Food and Drug Administration, a qualified representative of the drug manufacturer, and the Radiation Therapy Oncology Group. If we publish the information we learn from this study in a medical journal, you will not be identified by name.

RIGHT TO WITHDRAW:

Whether or not you take part in this study will not affect your future relations with your doctors. If you decide to take part, you are free to stop whenever you want to. You understand that you have the right to refuse to participate in this research study if you so desire without any fear of prejudice to additional treatment for yourself. In addition, you understand that you may refuse to continue on this study, at any time after the start of therapy, without fear of prejudice to additional treatment you may need. You recognize that you have received a copy of this consent form, and your signature indicates that you have volunteered to participate in the study having read the information provided to you.

VOLUNTARY CONSENT:

You certify that you have read the preceding or it has been read to you and that you understand its contents. Any questions you have pertaining to the research or research related injuries have been and will be answered by Dr. Nelson Adamson, who may be reached by phoning the office at (906) 776-5975. During evenings, weekends, or holidays you may phone Dickinson County Health System at 906-774-1313, and request to speak with the radiation therapist on call. Any questions you have concerning your rights as a research subject will be answered

by the Patient Advocate at Marquette General Hospital, who may be reached by phoning (906) 225-3433. You will be given a copy of this consent form.

Your signature below means that you have freely agreed to participate in this investigational study.

Patient's Signature

Date

Signature of person conducting
Informed consent discussion

Date

I certify that the nature and purpose, the potential benefits, and possible risks associated with participation in this research study have been explained to the patient indicated, and that any questions about this information have been answered.

Investigator's Signature

Date

Your signature below means that you do not wish to participate in this investigational study.

Patient's Signature

Date

Signature of person conducting
Informed consent discussion

Date

Investigator's Signature

Date

IRB approved consent form 12/12/07