

**MARQUETTE GENERAL HEALTH SYSTEM**  
Regional Medical Center

**CONSENT TO PARTICIPATE IN AN INVESTIGATIONAL STUDY**

**TITLE: RTOG 0435 - A Randomized, Phase III, double-blind, placebo controlled study to evaluate the efficacy and safety of Palifermin (NSC# 740548; IND #6370) for the reduction of oral mucositis in patients with locally advanced head and neck cancer receiving radiation therapy with concurrent chemotherapy (followed by surgery for selected patients).**

**INVESTIGATORS:** Nelson Adamson, MD  
Radiation Oncology  
Dickinson County Healthcare System  
1721 S. Stephenson Avenue  
Iron Mountain, MI 49801

Daniel Arnold, MD  
Sheetal Acharya, MD  
Adnan Alkhalili, MD  
Gustavo Morel, MD  
Mohammad Al-Nsour, MD  
Irena Sachelaire, MD  
Aaron P. Scholnik, MD  
Shahid Shekhani, MD  
1414 W. Fair Avenue  
Marquette, MI 49855

This is a clinical trial, a type of research study. Your study doctor 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 head and neck cancer for which you are receiving radiation therapy and chemotherapy.

**Why is this study being done?**

Painful sores in the mouth are a common side effect of radiation therapy and chemotherapy. There is no current treatment to prevent these sores. The purpose of this study is to compare the effects, good and/or bad, of a drug, palifermin, with placebo to find out if palifermin prevents these sores.

Palifermin is a drug that speeds up the growth of epithelial cells, cells that line the inside and outside surfaces of the body, such as the mouth, throat, or skin. Palifermin has been approved by the FDA for patients that are receiving radiation therapy and chemotherapy for cancer of the blood or lymph nodes. It has not been approved for patients with head and neck cancer. Palifermin is considered an investigational drug in this study.

The placebo looks like palifermin but is not an active medicine. In this study, you will get either palifermin or the placebo. You will not get both.

**How many people will take part in the study?**

About 298 people will take part in this study.

## 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.

- A physical exam
- Evaluation of the lining of your mouth and throat
- Evaluation of your ability to make saliva and the dryness of your mouth and throat
- An evaluation of your weight and the calories and fluids you are receiving each day
- A chest X-ray or CT (Computed Tomography) scan of your chest; a CT scan is a study using x-rays to look at one part of your body
- CT scan or MRI (Magnetic Resonance Imaging) of your tumor; an MRI is imaging using a strong magnetic field to look at one part of your body
- Blood tests
- For women able to have children, a pregnancy test
- Testing of your blood for antibodies (natural materials produced by your body to fight unfamiliar matter) to palifermin

Development of antibodies (natural materials produced by your body to fight unfamiliar matter) was reported in 2% of patients who received palifermin. These antibodies could decrease the effect of palifermin in the body, but it did not in these patients, and the antibodies did not make these patients unhealthy.

**During the study**, you will need these tests and procedures once a week during radiation therapy and chemotherapy to see how the study is affecting your body:

- Physical exam
- Blood tests

In addition, you will need these tests and procedures twice a week during radiation therapy and chemotherapy to see how the study is affecting your body

- Evaluation of the lining of your mouth and throat
- The study doctor or research nurse will ask you how much pain medicine you are taking each day.

### **3 Days before the second and third dose of chemotherapy**

- Blood tests

**All patients in this study will receive 7 weeks of radiation therapy and chemotherapy (cisplatin) while they receive palifermin or placebo.** Radiation therapy will be given 5 days a week, Monday through Friday. Each radiation treatment will take about 5-10 minutes. You will receive cisplatin through your vein on days 1, 22, and 43 before RT. Receiving the cisplatin takes about 30 minutes.

**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 doctor can choose the group you will be in, and neither you nor your doctor will know in which group you are placed. You will have an equal chance of being placed in any group.**

**If you participate in this study**, you will receive up to 8 doses of palifermin or placebo through your vein. Receiving a dose takes about 5 minutes. You will receive palifermin or placebo the Friday before your radiation therapy and chemotherapy begin, then on the next 3 Fridays, days 5, 12, and 19. If you still have sores in your mouth at the end of radiation treatment, you also will receive palifermin or placebo on the last Friday of radiation therapy and chemotherapy, then after completing therapy, once a week for 3 weeks or until the sores in your mouth have gone away, up to an additional 3 doses.

### **When you are finished taking palifermin or placebo:**

- For about 8 weeks after radiation treatment and cisplatin has ended, the study doctor will examine the lining of your mouth and throat twice a week.
- At 6-9 weeks and then once a year for years 1- 5, you will have a CT scan or MRI of the head and neck to see if your cancer has responded to chemotherapy and radiation therapy, or is stable, or is progressing. Patients with

remaining large tumors after chemotherapy/radiation will have surgery to remove the cancer, if it is found that surgery can be done to remove the remaining cancer. The study doctor and surgeon will discuss the need for this re-evaluation and surgery with these patients.

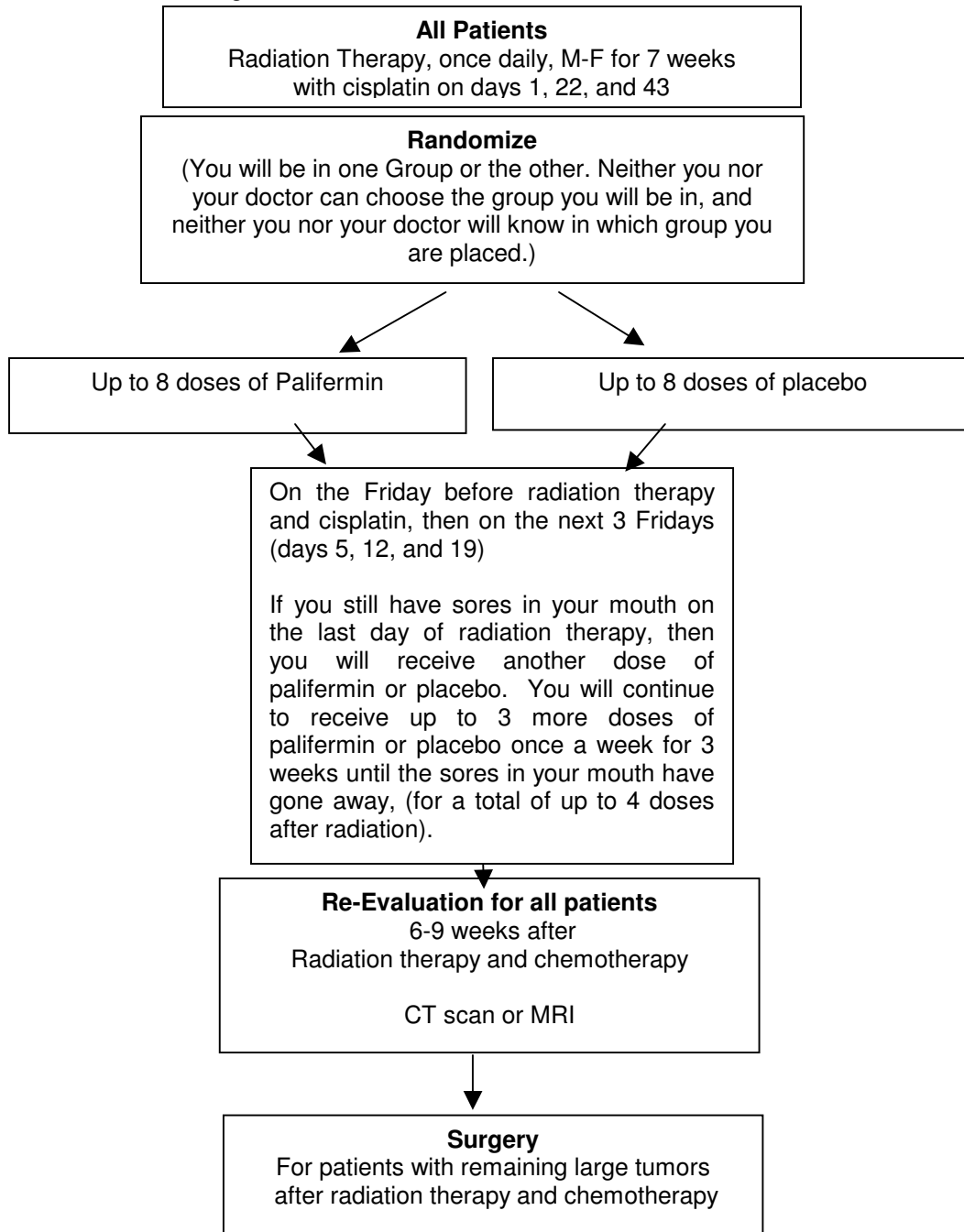
- For 4 months from the start of treatment, you will be asked to write down in a diary how much pain medicine you take each day. You will bring the diary with you to each follow-up visit with the study doctor.

**In follow-up visits**, you will need these tests and procedures. You will be seen in follow-up visits at 6-9 weeks, every 3 months for year 1, every 4 months for year 2, every 6 months for years 3-4, then once a year for years 5-10.

- A physical exam
- Evaluation of the lining of your mouth and throat
- Evaluation of your ability to make saliva and the dryness of your mouth and throat
- An evaluation of your weight and of the calories and fluids you are receiving each day

## Study Plan

Another way to find out what will happen to you during the study is to read the chart below. Start reading at the top and read down the list, following the lines and arrows.



## How long will I be in the study?

You will receive treatment for about 10 weeks. You will receive 4 doses of palifermin or placebo during the 7 weeks of radiation therapy and cisplatin. After completing radiation therapy and cisplatin, if you still have sores in your mouth, you will receive up to 4 more doses of palifermin and placebo, once a week for 4 weeks or until the sores in your mouth have gone away.

After radiation therapy and cisplatin are finished, you will be seen in follow-up visits twice a week for about 8 weeks, if you still have sores in your mouth. In addition, at 6-9 weeks after radiation therapy and cisplatin is finished, you will be re-evaluated to see if your cancer has responded to radiation therapy and chemotherapy.

After you are finished taking palifermin or placebo, the study doctor will ask you to visit the office for follow-up exams. You will be seen in follow-up visits every 3 months for year 1, every 4 months for year 2, every 6 months for years 3-4, then once a year for years 5-10.

## 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 palifermin or placebo can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what followup 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, doctors 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. Some medicines for painful sores in the mouth besides palifermin are allowed in this study. Some medicines, such as mouthwash solutions or Gelclair®, are not allowed. If you participate in this study, the study doctor will talk to you about these other medicines.

Many side effects go away soon after you stop radiation therapy, cisplatin, and palifermin/placebo. In some cases, side effects can be serious, long lasting, or may never go away. There also is a risk of death.

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

### Risks Related to Radiation Therapy When Given in Combination With Cisplatin

#### Very Likely

- Sores in the mouth and throat that are likely to interfere with swallowing
- Dryness of the mouth or altered taste that may be permanent
- Temporary hair loss (of the face/chin/neck)
- Tanning, redness, or blistering or peeling of skin in treatment area
- Loss of teeth, or cavities in teeth, if strict dental care is not followed
- Hardness and tightness of the skin and muscles of the head and neck
- Loss of appetite
- Weight loss

### **Less Likely, But Serious**

- Permanent hair loss (of the face/chin/neck)
- Decrease in function of thyroid gland which may require you to take thyroid replacement medicine to prevent you from feeling tired or sleepy
- Difficulty with swallowing and eating for which you might need a long term or permanent feeding tube
- The possibility of inhaling food and/or liquids into the lungs, which could also result in pneumonia
- Serious ear infections and/or hearing loss
- Damage to the spinal cord leading to permanent weakness and/or symptoms like a “stroke”

### **Rare**

- Severe damage to the jawbone and/or voice box which could require major surgery to correct or even to remove the jaw bone and/or voice box

### **Risks and Side Effects Related to Cisplatin**

Cisplatin is a standard (not experimental) treatment for head and neck cancer. The side effects listed below under “Likely” are expected to occur. The study doctor or your hospital may want to admit you to the hospital overnight to treat these side effects.

### **Likely**

- Tiredness and/or general weakness
- Nausea and/or vomiting
- Decrease in white blood cell count, which may increase the risk of infection, decreased healing, and/or bleeding
- Decrease in red blood cell count, which may result in anemia, tiredness, and/or shortness of breath
- Decrease in platelets, the cells in the blood that help blood clot normally
- Loss of appetite and/or weight loss
- Ringing in the ears and/or hearing loss

### **Less Likely**

- Decrease in the kidneys’ ability to handle the body’s waste, which may be permanent
- Changes in electrolytes, which may result in tiredness, cramps, and/or numbness and tingling
- Involuntary movements, restlessness, muscle cramps, and/or loss of coordination
- Numbness and tingling in the fingers, hands, toes, and feet

### **Rare**

- Hair loss
- Loss of taste
- Seizures
- Loss of muscle or nerve function, which may result in weakness
- Allergic reactions, which can involve flushing, difficulty breathing, irregular heartbeat, low blood pressure, and can even be life threatening
- Another cancer called acute leukemia

### **Risks and Side Effects Related to Palifermin**

Palifermin is a drug that speeds up the growth of epithelial cells, cells that line the inside and outside surfaces of the body, such as the mouth, throat, or skin. Whether or not palifermin could cause growth of your cancer is not yet known. In laboratory and animal studies, there is evidence that palifermin did speed up the growth of some cancers, but the dose of palifermin used in these studies was higher than the recommended dose for humans. A study of palifermin given to patients with head and neck cancer is ongoing and after four years, this study has not shown that palifermin causes growth of tumors or decreases patients’ survival.

In this study, the study doctor will be carefully checking the effects of your treatment (radiation therapy and chemotherapy) and the effects of palifermin on you and on your cancer. In addition, many parts of the body have epithelial cells, such as the milk-producing glands or parts of the eye. Since palifermin could speed up growth of these cells, there could be unexpected side effects.

### **Likely**

- Skin reactions, which can occur on all areas of the body and can include rash, reddening of the skin, flushing, itching, increased sensitivity of the skin, and swelling due to fluid in the tissue
- Discoloration, swelling or thickening of the tongue and lining of the mouth
- Loss of taste, which is temporary
- Tingling of the lips and mouth
- Reddening of the lining of the mouth
- Temporary increase in blood levels of certain salivary gland enzymes that is unlikely to cause serious symptoms or problems.

### **Less Likely**

- Headache
- Swelling around the eyes

### **Less Likely, but Serious**

- Difficulty breathing

### **Rare but serious**

- Allergic reactions, which can involve flushing, difficulty breathing, irregular heartbeat, low blood pressure, and can be life threatening; patients who have had allergic reactions to *E. coli*-derived products, such as Nutropin®, Neupogen®, Humulin®, Roferon®, Neumega®, Neulasta®, Intron-A®, and/or Betaseron® should not participate in this study.

### **Other possible serious side effects**

- Swelling of the back of the throat, tongue, windpipe, or around a surgical opening into the neck to allow the passage of air were reported in some patients with head and neck cancer receiving palifermin. This swelling might have led to breathing difficulties in one patient. These patients had undergone surgery to remove their cancer before starting radiation therapy and chemotherapy. The swelling was temporary and started after the patients began radiation therapy. Also, one of these patients decided to stop palifermin as the patient was making too much saliva. These side effects may have been related to palifermin.
- Protein in the urine was reported in some patients with colorectal cancer receiving palifermin. It is not yet known if this was related to the palifermin or to the patients' medical conditions.
- High blood pressure was reported in cancer patients undergoing a transplant and receiving palifermin. This was temporary and also was reported in the patients who received placebo.

### **Risks Associated with Neck Surgery**

Patients with remaining large tumors after RT/chemotherapy will have surgery to remove the cancer, if it is found that surgery can be done to remove the remaining cancer. The study doctor and surgeon will discuss the need for surgery with you. You will need to review and sign a separate permission form from your doctor/hospital for this surgery.

The serious risks of surgery are infection, bleeding, poor healing of the skin and/or muscles in the neck, clots in the legs and/or lung, pneumonia, heart attack stroke, and/or death.

These risks may be more likely or severe for people in this study than for someone having neck surgery without having had chemotherapy and/or radiation therapy before surgery.

**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 who are able to have children will have a pregnancy test before beginning treatment. 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.

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. While doctors hope that palifermin will be useful against painful mouth sores, there is no proof of this yet. We do know that the information from this study will help

doctors learn more about palifermin as a treatment for this side effect of cancer treatment. 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 painful mouth sores without being in a study
- Taking part in another study
- Getting no treatment

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

## **Will my medical information be kept private?**

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 Radiation Therapy Oncology Group
- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people
- Amgen, Inc., the manufacturer of palifermin and placebo

## **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. 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.

Amgen, Inc. is supplying palifermin and placebo at no cost to you. However, you or your health plan may need to pay for costs of the supplies to administer the drug and for the personnel who give you the palifermin or placebo.

**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.**

### **COSTS AND PAYMENTS:**

You understand that the RTOG Group and Marquette General Hospital 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 RTOG 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.

### **WHOM DO I CALL IF I HAVE PROBLEMS OR QUESTIONS?**

If injury occurs as a result of this research, treatment will be available. You understand, however, you will not be provided with reimbursement for medical care other than what your insurance carrier may provide nor will you receive other compensation. For more information concerning the research and research-related risks or injuries, you can notify Dr. \_\_\_\_\_ the investigator in charge at Dickinson County Health System at 906-776-5975. During evenings, weekends, and holidays you may phone Dickinson County Health System at 906-774-1313 and ask for the Radiation Oncologist on call. In addition, you may contact the Patient Advocate at Marquette General Hospital at (906) 228-9440 for information regarding patients' rights in research studies.

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

It is important that you tell your study doctor, \_\_\_\_\_, if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him/her at \_\_\_\_\_.

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 meeting regularly 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.

### **WHOM DO I CALL IF I HAVE PROBLEMS OR QUESTIONS?**

In the event that physical injury occurs as a result of this research, facilities for treatment of injury will be available; however, you will not automatically be provided with reimbursement for medical care or other compensation. For more information concerning the research and research-related risks or injuries, you can notify Dr. \_\_\_\_\_, or his/her associates, who may be reached by phoning the office at \_\_\_\_\_. During the evenings, weekends, or holidays you may phone Marquette General Hospital at (906) 228-9440, and request to speak with the radiation oncologist on call. You can also call the Patient Advocate at Marquette General Hospital at (906) 228-9440, if you have any questions, comments, or concerns about the study or your rights as a research subject.

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

**You can say "yes" or "no" to each of the following studies. 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 and the side effects of cancer treatment.

You will be asked to complete 2 questionnaires, the MD Anderson Symptom Inventory and the Brief Pain Inventory, at the following times: At your first visit, twice a week during radiation therapy and until the sores in your mouth are healed or for 8 weeks after radiation therapy. Then you will be asked to complete 1 of the questionnaires at 12 months from the start of treatment. It takes about 5 minutes to fill out each questionnaire.

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 study, the only thing you will be asked to do is fill out the two questionnaires. You may change your mind about completing the questionnaires 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.**

**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.**

### **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. \_\_\_\_\_ or his/her associates, who may be reached by phoning the office at \_\_\_\_\_. During evenings, weekends, or holidays you may phone Marquette General Hospital at (906) 228-9440, and request to speak with the radiation oncologist 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) 228-9440. 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 10/11/06