
MARQUETTE GENERAL HEALTH SYSTEM

Regional Medical Center

CONSENT TO PARTICIPATE IN AN INVESTIGATIONAL STUDY

TITLE: ECOG E5204 - Intergroup Randomized Phase III Study of Postoperative Oxaliplatin, 5-Fluorouracil and Leucovorin vs Oxaliplatin, 5-Fluorouracil, Leucovorin and Bevacizumab for Patients with Stage II or III Rectal Cancer Receiving Pre-operative Chemoradiation

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You are being asked to take part in this study because you have rectal cancer and have already received chemotherapy, radiation and surgery for your disease. You may benefit from additional treatment. This is a type of clinical trial (research study). Clinical trials include only patients who choose to take part. Please take your time to make your decision and discuss it with your friends and family.

WHY IS THIS STUDY BEING DONE?

To compare the effects (good and bad) of a combination of chemotherapy drugs, when given with and without a new drug, bevacizumab, after patients with stage II or stage III rectal cancer have had pre-operative chemoradiation. To date, there have been very few studies of different combinations of chemotherapies for patients with rectal cancer, who have already had surgery and radiation. This study will compare the overall survival in patients with clinical stage II and stage III rectal cancer who received preoperative chemoradiation and surgery and will compare the investigational treatment combination of oxaliplatin, fluorouracil and leucovorin with or without bevacizumab. The standard of care for patients with stage III colon cancer is post-surgery chemotherapy with oxaliplatin, fluorouracil and leucovorin; however, this therapy has not been evaluated in patients with surgically-removed rectal cancer. The chemotherapy regimen chosen for this study is based on the results of the colon cancer adjuvant studies with the same drugs.

The chemotherapy drugs given in this study are 5-fluorouracil (5-FU), leucovorin and oxaliplatin. We want to see if adding bevacizumab to the other cancer-fighting agents is better for treating rectal cancer patients. We also want to see if adding bevacizumab will help prevent the cancer from coming back.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

About 2100 people in the United States and Canada will take part in this study.

WHAT IS INVOLVED IN THIS STUDY?

This is a randomized study, which means that the two chemotherapy treatment combinations are compared with each other to find out if one is better. If you agree to enter this trial, you will be randomly assigned to receive one of the two chemotherapy combinations. You have an equal chance of an assignment to either one. Random assignment helps to make the results of the research more scientifically sound. Neither you nor your doctor will have a say as to which group you are assigned to, but both you and your doctor will be informed as to which treatment you will receive. You will be assigned to one of the following arms:

Arm A – FOLFOX (acronym commonly used to refer to the following regimen) - this is a two-day treatment given every 2 weeks for a total of twelve 2-week cycles. Medications are given before chemotherapy to prevent nausea and vomiting. All of the chemotherapy drugs will be given intravenously (through a vein). Oxaliplatin is given over 2 hours; leucovorin is given over 2 hours, followed by 5-FU (5-fluorouracil) given as a quick infusion, followed by 5-FU given as a constant infusion through a portable pump over the next 46 hours.

Arm B – FOLFOX + Bevacizumab

All of the chemotherapy drugs will be given intravenously (through a vein). Bevacizumab is given over 30-90 minutes, before the oxaliplatin, leucovorin and 5-FU. Oxaliplatin is given over 2 hours; leucovorin is given over 2 hours, followed by 5-FU (5-fluorouracil) given as a quick infusion, followed by 5-FU given as a constant infusion through a portable pump over the next 46 hours.

Please note, if you were randomized to the preoperative oxaliplatin arm of NSABP R-04, or if you received oxaliplatin with your radiation and did not participate on NSABP R-04, you will have already received 3 cycles of oxaliplatin and, therefore, on this study you will receive only 9 cycles of oxaliplatin. After 9 cycles, the chemotherapy will continue as planned without the oxaliplatin.

If you take part in the study, you will have the following tests and procedures. Some of the tests required for this study would be done even if you did not participate in the study.

- Female patients (of childbearing potential) will have a pregnancy test.
- You will receive a complete physical exam and be seen by a physician at the beginning of each cycle of treatment.
- Blood tests, along with chest x-rays, CT scans or MRI will be performed to evaluate your health status.

In addition, you will be asked to fill out brief forms with questions about your bowel function. This will take about 10 to 15 minutes.

HOW LONG WILL I BE IN THE STUDY?

The actual treatment period on the study is approximately 6 months. We would like to keep track of your medical condition for a period of 10 years after entering the study, to look at the long-term effects of the treatment. You may stop participating at any time; however, we encourage you to talk to your study doctor first.

WHAT ARE THE RISKS OF THE STUDY?

While on the study, you are at risk for the following side effects. The chemotherapy may cause some, all or none of the side effects listed. You should discuss these with your doctor. There may also be other side effects that we cannot predict. Other drugs will be given to make side effects less serious and less uncomfortable. Many side effects go away shortly after the chemotherapy drugs are stopped, but in some cases side effects can be serious, long-lasting, permanent or life threatening. Death is rare, but possible.

Your physician will check you closely to see if any of these side effects are occurring and routine blood tests will be done to monitor the effects of treatment.

Oxaliplatin, Leucovorin and 5-Fluorouracil

Likely

- Lowered white blood cells (may make you more likely to get infections)
- Lowered platelets (may make you more likely to bruise or bleed)
- Lowered red blood cells (may make you feel tired or weak)
- Fatigue (feeling tired all the time)
- Nausea (feeling sick to your stomach) and vomiting (throwing up)
- Diarrhea (frequent bowel movements with loose, watery stools)
- Numbness or tingling in your hands and/or feet (may feel stronger if exposed to cold)
- Feeling of tightness or fullness in the throat, making it feel like it is difficult to breathe or swallow
- Soreness or redness where the drug is injected
- Temporary hair loss
- Pain and the risk of infection where the drugs are injected

- Mouth sores or sore throat, which may make swallowing difficult
- Sunlight sensitivity
- Nail changes, loss
- Constipation (having fewer and harder bowel movements)
- Dehydration (decreased fluid in the body because of diarrhea or inability to drink fluids)
- Appetite loss
- Skin darkening, hives, itchy dry skin
- Shortness of breathe
- Rash
- Fever
- Pain that could be in the belly, chest, bones, muscles or joints, along the spine and legs.
- Trouble sleeping
- Hearing loss
- Damage to the liver and kidneys
- Headache

Less Likely

- Hypoxia (a lower-than normal concentration of oxygen in the blood)
- Flu-like symptoms such as fevers, chills and muscle aches
- Watery eyes, runny nose
- High blood pressure
- Swelling in the arms and legs
- Changes in taste
- Upset stomach, heartburn, gas
- Temporary blockage or paralysis of the bowels, resulting in abdominal pain and cramping, which may prevent normal bowel movements.
- Changes in the salts in the bloodstream, such as phosphorous, calcium, magnesium, sodium and/or potassium
- Inflammation of the lungs
- Blistering on the palms of the hands and soles of the feet
- Dry mouth
- Hot flashes or flushing, (redness of face and neck)
- Cough
- Thrombosis/thrombus/embolism (vascular access-related)(blood clot)
- Hiccups
- Fluid collecting in the abdomen
- Vision changes (blurring) usually brief
- Allergic reaction (symptoms vary but difficulty breathing, upset stomach, nausea, vomiting, diarrhea, skin rash and/or itching are common)
- Temporary blindness
- Allergic rhinitis (including sneezing, nasal stuffiness, postnasal drip)
- Neuropathy; motor (weakness, numbness caused by malfunction of the nerves)
- Adult respiratory distress syndrome (ARDS) (respiratory failure)

Rare

- Confusion, memory loss, depression, anxiety or other mental changes
- Lack of balance (feeling as if you might fall down), dizziness,
- Change in your heart beat (rapid heart beat)
- Chest pain or heart attack
- Blood clot in the brain
- Slurred speech
- Infection
- Hoarseness, loss or alteration in voice, laryngitis
- Seizure or passing out
- Abnormal eye muscle movement, fluid in or around the eye
- Muscle spasms or loss of normal muscular contraction
- Changes in nerve function, lack of coordination
- Pain while peeing, inability to pee or frequent need to pee; blood in the urine
- Blood clots in the lungs, legs
- Abnormal liver function

Rare, but Serious

- Hemolytic Uremic Syndrome – a breakdown of red blood cells, low platelets and kidney failure together.

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- Pulmonary Fibrosis - lung problems such as cough, shortness of breath, trouble breathing, build-up of scar tissue in lungs; thickening and stiffening of lung tissue. Can be life threatening - tell your doctor right away if you experience any of these problems.
 - Tumor Lysis Syndrome – complication can occur when cancer cells are destroyed by treatment. Cell destruction may damage kidneys and change calcium levels, which may lead to kidney dialysis, usually on a short-term basis.
 - Disruption of blood proteins where bleeding and blood clots can occur at the same time, which could be life-threatening.
 - Bleeding from any source including stomach (throwing up blood or black stools), lung (coughing up blood), bowels (blood in the stool) or brain; which could be life-threatening.
 - Veno-occlusive disease – liver injury which leads to an enlarged liver, enlarged spleen, swelling in the abdomen and jaundice (yellowing of the skin); could be life-threatening.
 - Although very rare, it is possible that treatment-related side effects could result in death.
 - Visual changes (including temporary blindness, usually lasting less than 1 minute).
 - Cholecystitis (inflammation of the gallbladder)
 - Gastrointestinal – Other (pneumotosis intestinalis)(air in the bowel wall)

Bevacizumab

Likely

- High blood pressure (including dangerously high blood pressure called hypertensive crisis)
- Shortness of breath
- Abnormal levels of protein in the urine (which may indicate kidney damage)
- Mild to moderate bleeding in the gastrointestinal tract
- Nose bleeds
- Sores in mouth and/or throat
- Changes in taste
- Skin changes (including itching, rash, discoloration, ulcers or peeling)

Less Likely

- Clots in the arteries, including stroke or heart attack. When several studies were looked at together, problems due to clots in arteries were increased about two-fold (up to 4-5%) in patients receiving chemotherapy plus bevacizumab compared to chemotherapy alone (about 2%). Patients who were elderly and had a past history of clots in the arteries appeared to be at greater risk for these problems. Problems due to blood clots in the arteries were seen in about 2.9% of patients 65 or older receiving chemotherapy alone, and about 8.5% of patients 65 or older receiving bevacizumab with chemotherapy. Patients who were both 65 or older and reported a history of past problems with blood clots in their arteries appeared to be at even higher risk, although further study is required before an estimate of the risk can be provided. These conditions can be life threatening or fatal.
- Lowered white blood cell count (may make you more likely to get infections)
- Lowered platelet count that might interfere with clotting (may make you more likely to bruise or bleed)
- Lowered sodium and/or potassium levels that might make you feel weak or dizzy
- Changes in blood tests that indicate possible damage to the kidney

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- Gastrointestinal upset (which may include gas, constipation, diarrhea, nausea, vomiting, loss of appetite, heartburn, or dry mouth)
 - Cough
 - Watery eyes
 - Voice changes (hoarseness)
 - Headache
 - Pain
 - Weight loss
 - Confusion
 - Poor coordination and balance
 - Frequent urination (peeing)
 - Tiredness/weakness
 - Flu-like symptoms, such as fever, chills, stiffness and muscle aches

Rare but Serious

- Coughing up blood
- Worsening of any fluid within the tissues of the lung/lung problems
- Delay in wound healing or breakdown of a wound that had healed
- Heart problems (including irregular heartbeats, changes in blood pressure, fluid collections surrounding the heart, chest pain and possibly heart attack or heart failure)
- Bleeding in various parts of the body including the brain (stroke), the lungs (especially in lung cancer patients), the stomach, and the colon. This bleeding can lead to disability or death.
- Blood clots in the legs, lungs, or abdomen
- Serious stomach and/or bowel problems (such as the breakdown of tissue at the site where bowel is re-attached after removal of a tumor, formation of a hole in the stomach or bowel wall) which can lead to serious infection and require surgery to repair
- Bowel perforation - an opening occurs in the bowel wall, allowing bowel contents to spill into the abdomen. In addition to bowel perforation, perforation of other organs may occur.
- Breakdown in the surgical connection between two pieces of bowel (bowel anastomotic dehiscence). These events can be life-threatening.
- Blockage of the intestines and breakdown of the tissue in the intestines
- Reversible changes in liver function tests that may indicate liver damage
- Damage to the kidney
- Allergic reaction
- Infection
- Death
- Reversible Posterior Leukoencephalopathy Syndrome (RPLS) or similar leukoencephalopathy syndrome: RPLS is a medical condition related to leakiness of blood vessels in the brain and can cause confusion, blindness or vision changes, seizure and other symptoms, as well as changes in brain scans. This condition is usually reversible, but in rare cases, it is potentially life-threatening and may have a long-term effect on brain function.

Reproductive Risks

If you are pregnant or breast feeding, you cannot take part in this study. If you are a woman who has not gone through menopause, you will take a blood test to see if you are pregnant before you start treatment. If you are sexually active, your study doctor strongly recommends that you take precautions to avoid the possibility of becoming

pregnant because this therapy could kill or seriously damage an unborn child. Sexually active males are also strongly advised to use an accepted and effective method of contraception. For more information about risks and side effects, ask the researcher or contact your study doctor.

Patients in Arm B will receive drugs that may affect the way a woman's ovaries work and her ability to get pregnant. The drugs in this study can affect an unborn baby. Therefore, women should not become pregnant and men should not father a baby while on this study. (Men and women in Treatment Arm B should continue to take precautions for at least 3 months after their last dose of bevacizumab). Both male and female patients should ask about counseling and more information about preventing pregnancy. Female patients who think they might be pregnant, even though they practiced birth control, must notify the study doctor immediately. A pregnancy test may be performed. Male patients should also inform the study doctor immediately if their sexual partner(s) become pregnant while the patient is receiving treatment. Women should not breastfeed a baby while on this study, and, if they are in Treatment Arm B, for at least 3 months after their last dose of bevacizumab.

Doctors do not know for sure how bevacizumab may affect unborn children or children nursed by mothers who received bevacizumab. We do not know how long after stopping bevacizumab that you safely can become pregnant, father a child or nurse a child. A period of at least 3 months is recommended, although we do not know if this is actually best. It is best to discuss your concerns with your study doctor.

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

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you are taking part in this study, there may or may not be direct medical benefits to you. If you receive study treatment and do not show any benefit, your study doctor will discuss alternative treatments with you. You have been told that, should your disease become worse, should side effects become very severe, should new scientific developments occur that indicate the treatment is not in your best interest or should your doctor feel that this treatment is no longer in your best interest, the treatment will be stopped. Further treatment will be discussed.

We hope the information learned in this study will benefit other patients with rectal cancer in the future.

WHAT OTHER OPTIONS ARE THERE?

Instead of being in this study, you have the option of standard chemotherapy alone.

Your doctor can provide information about your disease and will be available to answer any questions about the research study.

WHAT ABOUT CONFIDENTIALITY?

This study is conducted by the Eastern Cooperative Oncology Group (ECOG). ECOG is a cancer group that conducts studies for the National Cancer Institute. Your study doctor is a member of ECOG or another group that is participating in this study. To help protect your privacy, ECOG has obtained a Confidentiality Certificate from the Department of Health and Human Services (DHHS).

With this Certificate, ECOG cannot be forced (for example, by court subpoena) to disclose information that may identify you in any federal, state or local civil, criminal, administrative, legislative or other proceedings. Disclosure will be necessary, however, upon request of DHHS for audit or program evaluation purposes.

You should understand that a Confidentiality Certificate does not prevent you or a member of your family from voluntarily releasing information about you or your involvement in this research. Please note that if an insurer or employer learns about your participation and obtains your consent to receive research information, then ECOG may not use the Certificate of Confidentiality to withhold this information. This means that you and your family must also actively protect your privacy.

Your identifiable health information is also protected by the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule, which was issued by the Department of Health and Human Services. Except as required by law, ECOG will not be able to disclose identifiable health information, expected to be collected in this study, to anyone other than you without your authorization, by a separate document you have signed or will be asked to sign.

Finally, you should understand that your study doctor and ECOG may take steps, including reporting to authorities, to prevent you from seriously harming yourself or others. The Certificate does not prevent the review of your research records under some circumstances by certain organizations. Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as:

- Eastern Cooperative Oncology Group (ECOG)
- National Cancer Institute (NCI)
- Cancer Trials Support Unit (CTSU) – an NCI-sponsored organization designed to increase accrual by providing greater access to phase III trials.
- North Central Cancer Treatment Group (NCCTG)
- National Surgical Adjuvant Breast and Bowel Project (NSABP)
- Food and Drug Administration (FDA)
- Other regulatory agencies and/or their designated representatives
- Drug manufacturers and/or their representatives, specifically
 - Genentech, Inc.
 - Sanofi-Aventis
- NCI Central Institutional Review Board (CIRB)
- Central laboratories and reviewers, tissue banks

WHAT ARE THE COSTS?

The Division of Cancer Treatment and Diagnosis, NCI will provide oxaliplatin free of charge for both arms of this study. Additionally, if you are assigned to the arm to receive bevacizumab, the Division of Cancer Treatment and Diagnosis, NCI will provide bevacizumab free of charge. Every effort will be made to ensure adequate supplies of oxaliplatin and bevacizumab are available to all participants. If these drugs become available commercially for this indication,

there is a remote possibility that you may be asked to purchase subsequent supplies. Your study physician will discuss this with you, should this situation arise.

Taking part in this study may lead to added costs to you or your insurance company. Please ask about any expected added costs or insurance issues. Medicare should be considered a health insurance provider. You may find the National Cancer Institute's guide "Clinical Trials and Insurance Coverage - A Resource Guide" helpful. Ask your doctor for a copy. It is also available on the world wide web at <http://www.nci.nih.gov/ClinicalTrials/Insurance>. Click on the printable version.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?

In the case of injury or illness resulting from this study, emergency medical treatment is available but will be provided at the usual charge. Although no funds have been set aside to compensate you in the event of injury or illness related to the study treatment or procedures, you do not give up any of your legal rights for compensation by signing this form.

You or your insurance company will be charged for continuing medical care and/or hospitalization.

You will receive no payment for taking part in this study.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or may leave the study at any time. Leaving the study, or choosing not to take part, will not result in any penalty or loss of benefits to which you are entitled.

We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

A Data Safety and Monitoring Board, an independent group of experts, will be reviewing the data from this research throughout the study. We will tell you about the new information from this or other studies that may affect your health, welfare, or willingness to stay in this study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or a research-related injury, contact your cancer doctor

_____ at _____.
NAME(S) *TELEPHONE NUMBER*

For questions about your rights as a research participant, contact the PATIENT ADVOCATE AT MARQUETTE GENERAL HEALTH SYSTEMS at 906-225-3183.

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.

COSTS AND PAYMENTS:

You understand that the study 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 study 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?

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 (906) 225-3922. During the evenings, weekends, or holidays you may phone Marquette General Hospital at (906) 228-9440, and request to speak with the oncology physician 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.

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 Southwest 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 or Marquette General Hospital. 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. _____ or his/her associates, who may be reached by phoning the office at (906) 225-3922. During evenings, weekends, or holidays you may phone Marquette General Hospital at (906) 228-9440, and request to speak with the medical 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 3/12/08
IRB approved Addendum#3 01/14/2009
IRB approved Update #4 00/00/00

ABOUT USING SPECIMENS FOR RESEARCH

If you participate in the clinical trial, we would also like samples of your tissue and blood to be used for research studies. These samples are referred to as “specimens”. These specimens and the health information collected during your participation in the clinical trial can be used to help doctors and scientists learn more about caring for and treating people with cancer and other diseases.

Below is some general information you should know before agreeing to allow the use of your specimens for research. After the general information there are descriptions of the research projects. Each project is described separately, including the types of specimens requested and how they are collected. Each description is followed by questions concerning your participation in the project. Your specimens will be used only for the projects in which you agree to participate.

You will not receive any payments for allowing your specimens to be used for these research studies, even if your specimens are used to help develop commercial products or tests someday. You or your insurance company will not be billed for the research studies performed using your specimens.

How Will My Specimens Be Used For Research?

There are two types of projects:

- Laboratory Research projects: These research studies are already planned and the project details are written in to the protocol. They are approved by ECOG and NCI, and have been reviewed by the researchers’ Institutional Review Boards.
- Future Research projects: Specimens are stored in central locations for use in future research. The type of projects they will be used for are not yet known. Future projects must be approved by ECOG and have been reviewed by the researchers’ Institutional Review Boards.

Researchers may study the differences and similarities of the cells or parts of the cells in the specimens, such as normal cells, tumor cells, proteins, and genetic material. The level of drug in the specimens may be studied. Some projects may study characteristics that are passed on in families (inheritable). The study of inheritable traits is a type of genetic research. To better understand the results, the researcher may compare the test results to the information collected from your participation in the clinical trial (such as your age, side effects you experience, and your cancer’s response to treatment).

Additional information on the importance of donating your specimens for research and how specimens are used for research can be found on the patient advocacy website (www.researchadvocacy.org) and on the NCI website at www.cancer.gov/clinicaltrials/.

Where will my specimens be stored and who has access to them?

If you agree to allow your specimens to be used for the research projects, your specimens will be sent to research laboratories for testing. After these tests are completed, the researchers will send any left over specimens to a repository (bank) where, if you agree, they will be stored for use by other researchers. The stored specimens will be kept indefinitely or until they are used up.

Because your specimens are valuable, researchers must present their projects for review and approval to scientific reviewers appointed by the Eastern Cooperative Oncology Group. Any research done on the specimens must also be reviewed by the researcher’s Institutional Review Board (a group of people who review the research to protect patient rights). Some projects may also require approval by the National Cancer Institute (NCI).

Will personal information be associated with the specimens?

The specimens sent to research laboratories and repositories will have some identifying information, such as initials and where the specimens were collected. To protect your identity, your specimens and any related information will receive a unique identification code. Researchers approved to use the specimens for future research will only receive the code that is attached to your specimen. Any information from your research records that is approved to go to a researcher will also receive a code.

Any research or information that is published, presented at scientific meetings or made public in any other way will use only coded information.

What are the risks?

There are very few risks to you if your specimens and data are used for this type of research. The greatest risk, although rare, is the loss of confidentiality caused by unauthorized release or misuse of information from your research records.

We will do everything possible to make sure that the information in your research records are kept private.

Risk from participating in genetic research: Your genetic information is unique to you. You do share some genetic information with your family members. Although rare, there are examples where health insurers or employers have denied insurance or employment based on results from genetic testing. Many states currently have laws to protect against genetic discrimination by employers or insurance companies. Currently there is no federal law that prohibits such misuse or discrimination.

How we will address these risks: We have several safeguards in place to prevent misuse of research results by any third party including insurers or employers: your research results will not be sent to you or your doctor and will not be placed in your medical record; insurers or employers will not be authorized to view any research records; and all information will be coded. As stated before, we also have a Certificate of Confidentiality from the US government, which protects your information from forced disclosure by civil, criminal, administrative, legislative or other proceeding. We believe that the risks to you and your family are very low.

Benefits

The research that may be done with your specimens will probably not benefit you directly. It may help researchers learn more about what causes cancer and other diseases, how to prevent them, and how to select the most appropriate treatment for future patients who have these diseases.

Changing your mind about letting us use your specimens

If at any time you decide you no longer want your specimens used for research, please give your doctor or study nurse a signed note stating your decision. They will contact ECOG and tell us about your decision.

If your specimens were already sent from the repository and are being used for a project when you withdraw your consent, your specimens and accompanying data will still be used for that approved project. Once you choose to end your participation, no further specimens or related information will be sent to researchers from the repository for any new research projects.

Specimens will NOT be returned to you.

Voluntary Participation

The choice to participate in the optional laboratory research projects or to allow your specimens to be stored for future research is completely up to you. **No matter what you decide to do, your decision will not**

affect your medical care. You can participate in the treatment part of the study without participating in these research projects.

Please read the research study descriptions below, review the questions carefully and circle “Yes” or “No”. If you circle “Yes”, you are indicating you understand:

- Coded information collected from your medical records may be given to researchers to perform these studies.
- The research results from your specimens will not be given to you or your doctor, they will not be placed in your medical record and they will not affect your medical care.
- Your specimens may be used in genetic research.
- The risks associated with allowing your specimens to be used in research, including the possible risks associated with genetic research.
- You will not receive any payment for the use of your specimens for these projects. You or your insurance will not be billed for any of these research studies.
- That at any time, you can end your participation in the projects and any remaining specimens or information will not be used for new research.

If you do not agree with any of the statements above, indicate “No” to ALL the questions below.

If you have any questions, please talk to your doctor or nurse, or call the Research Department at 906-225-6995.

LABORATORY RESEARCH STUDIES

This study includes laboratory tests that will analyze small samples of your tissue. If you participate in the laboratory studies associated with this protocol, some of the leftover tissue used to diagnose your disease will be sent to a research laboratory for analysis. No additional procedures will be done to obtain this tissue. Researchers will be performing these tests in order to better understand the biology of rectal cancer. They hope these studies will help them better understand this type of cancer. The results of these tests will not be sent to you or your doctor and will not be used in planning your care.

Please review the points listed in the “Voluntary Participation” section above, then read the questions below and circle “Yes” or “No”.

I agree to participate in the laboratory research studies that are being done as part of this clinical trial.

Yes No

PHARMACOGENETIC LABORATORY STUDIES

When a patient receives a treatment for cancer, how effective the treatment may be depends on how the drugs act in both normal and cancer tissue. People differ in how their bodies breakdown and absorb drugs. Side effects are often different between patients. Different cancers also may respond differently to the same drug. It is important to understand the differences between people and cancers so that patients can be treated with the most effective treatment with the fewest number of side effects.

Pharmacogenetics is the study of genetic differences (which may be inheritable) that effect response to drugs. Specimens for these types of studies will be collected once or twice.

The purpose of the laboratory studies described below is to investigate how oxaliplatin affects your cancer and to understand some of the side effects caused by the treatment. About 5000 patients with colorectal cancers and who are being treated with oxaliplatin are being asked to participate in theses studies.

PHARMACOGENETIC STUDIES

The studies will look at differences in certain proteins and genes (DNA) that are known to be affected by or involved in processing oxaliplatin. Also, some studies will be general search to look for other markers or genes that may predict response or toxicity to oxaliplatin. If you agree to participate in these studies, one of blood (about 1 tablespoon) will be collected (usually before you start treatment, but may be collected anytime). The samples of your tumor tissue, if available, may also be used in these studies. An additional biopsy is not necessary.

I agree to participate in the protein and DNA studies that are being done as part of this clinical trial.
(If you do not want your specimens used for genetic research, answer "No")

Yes No

USING SPECIMENS FOR FUTURE RESEARCH

We would like to keep some of your specimens for future research.

If you participate in the laboratory research studies or the pharmacogenetic studies associated with this protocol, this means any specimens left over from theses studies will be stored for future research. If you do not participate in theses laboratory studies, we would still like to have some of your tissue from a previous biopsy or surgery to use for future research. Although most future research studies will focus on cancer, some research projects may also include other diseases, such as heart disease, diabetes, or Alzheimer's disease.

As indicated above, the specimens will only be given to researchers approved by scientific reviewers appointed by the Eastern Cooperative Oncology Group. Any research done on the specimens must also be reviewed by the researcher's Institutional Review Board.

Please review the points listed in the "Voluntary Participation" and the risks associated with donating your specimens for research (including genetic research) outlined in the section above. Then read the questions below carefully and circle "Yes" or "No".

My specimens may be kept for use in research to learn about, prevent, treat, or cure cancer.

Yes No

My specimens may be kept for research about other health problems (for example: causes of diabetes, Alzheimer's disease, or heart disease).

Yes No

PERMISSION TO CONTACT YOU IN THE FUTURE

We request your permission to contact you in the future about taking part in more research studies. If you agree and we decide to contact you in the future, we will first contact your doctor or some one at your hospital. They will tell you why we would like to contact you and, if you agree, they will send us your contact information. We will not attempt any direct contact without obtaining this second permission from you.

Someone from this institution may contact me in the future to ask me to take part in more research.

Yes No

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or a research-related injury, contact your cancer doctor

_____ at _____.

For questions about your rights as a research participant, contact the Patient Advocate at Marquette General Hospital at 906-225-3183.

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/>.

SIGNATURE

I agree to take part in this study _____

Participant _____ Date _____
