NCT03781323

Consent Form

Neoadjuvant FOLFOX therapy and active surveillance with selective use of radiation in locally advanced rectal cancer: A Phase II Study

Principal Investigator: Richard Dunne, M.D.

This consent form describes the research study, what you may expect if you decide to take part and important information to help you make your decision. Please read this form carefully.

Key Information

- Being in this research study is voluntary – it is your choice.
- You are being asked to take part in this study because you have locally advanced rectal cancer without metastatic disease
- The purpose of this study is to determine if chemotherapy and short course radiation alone will adequately treat your cancer without the use surgery.
- Your participation in this study will last for about 2 years.
- Procedures will include blood work, administration of chemotherapy, CT scans and MRI and sigmoidoscopy.
- There are risks from participating.
    - The most common risks are fatigue, nausea, diarrhea and nerve damage.
    - One of the most serious risks is life-threatening infection. See the "Risks of Participation" section in this consent form for more information. You should discuss these risks in detail with the study team.
- You might not benefit from being in this research study. The potential benefit to you might be better quality of life if you are able to avoid surgery.
- If you do not want to take part in this study, you would proceed with standard treatment of chemotherapy and radiation followed by surgery.

Introduction:

You are being asked to take part in this study because you have locally advanced rectal cancer without metastatic disease, normally treated with chemotherapy and radiation prior to surgical resection of tumor, followed by additional chemotherapy after surgery.

This study is being conducted at the University of Rochester's James P. Wilmot Cancer Institute and is being directed by Dr. Richard Dunne.

Purpose of Study:

The purpose of this study is to evaluate if giving a chemotherapy regimen called FOLFOX, plus short course radiation used in the treatment of rectal cancer, may be able to completely treat a rectal tumor without the use of surgery.

The standard treatment for a localized rectal tumor is to treat with chemotherapy and radiation for approximately 5 weeks prior to surgery, then surgically remove the tumor, followed by additional chemotherapy with FOLFOX for a combined total of 4 months of chemotherapy. Though treating with chemotherapy, radiation, and surgery may be curative for rectal cancer, receiving all of these treatments may increase the likelihood of long term side effects. Radiation therapy can cause local irritation to treatment sites, causing diarrhea and harm to skin, and it can cause healing complications at the site of surgery. Radiation and surgery can cause sexual dysfunction, bowel and bladder dysfunction, or small bowel obstruction. Chemotherapy can cause low blood cell counts, numbness and tingling in fingers and toes (neuropathy). All of these treatments can cause gastrointestinal symptoms and fatigue.

This study offers chemotherapy with FOLFOX, given for up to 12 cycles, once every two weeks for a total of 24 weeks of therapy. Participants who respond well to chemotherapy will be watched closely but may be able to avoid both radiation and surgery. Participants who do not respond well to chemotherapy and radiation will require surgery. The study doctor will explain more to you given your specific cancer findings.

Schedule of Events:

- Prior to Treatment- Baseline Assessments including physical examination, blood work, EKG, MRI, CT and sigmoidoscopy will be performed to determine if you qualify for the study. Imaging will not be repeated if it was completed during the baseline window.
- On Day 1 of each chemotherapy cycle participants will receive FOLFOX chemotherapy
- Following 6 cycles of FOLFOX there will be a reassessment with sigmoidoscopy MRI and CT scans
- Patients with an adequate response will proceed with 4-6 additional cycles of FOLFOX
- Patients who do not have an adequate response will be removed from study and followed for survival.
- Following 10-12 cycles of FOLFOX there will be a reassessment with sigmoidoscopy MRI and CT scans.
- Patients who have a complete response or near complete to treatment will have short course radiation and then will begin surveillance.
- Patients who do not have a complete response to treatment will have short course radiation followed by surgery.
- Patients who are in surveillance will be evaluated sigmoidoscopy MRI and CT scans every 6-12 months for 5 years, in total participants will have up to nine (9) MRI and CT scans.

- Participants will also be asked to complete a quality of life questionnaire at up to eleven intervals during the study.

Description of Study Procedures:

If you choose to participate in this study, you will be asked to have initial testing prior to beginning the study. This will include blood work, up to nine MRI/CT scans, rectal examination with sigmoidoscopy or proctoscopy (the insertion of a rigid scope into the rectum to evaluate for a cancer) by a surgical oncologist if you are female, you will have a pregnancy test. The specific imaging tests that will be required include both CT scans and MRI scans. You may have had some of these studies completed prior to enrolling in this study; if so, you may not need to have them repeated. All imaging scans that are completed will be performed as part of the standard of care.

In addition, you may be asked to provide an additional blood sample to be used to identify potential markers of rectal cancer. This blood work would be collected at the same time as other standard blood draws and is optional.

Once testing requirements are complete and you have been found eligible to participate, you will begin treatment. You will have six cycles of FOLFOX therapy (5-fluorouracil, leucovorin, and oxaliplatin) given as IV therapy every two weeks, as well as close monitoring by your medical oncologist. After the first six cycles, you will be evaluated for response with another examination by your surgical oncologist and imaging to make sure the chemotherapy is working against the cancer.

If the cancer is shrinking, you will proceed with four to six additional cycles of FOLFOX chemotherapy. If the cancer appears to have not changed or is growing, it is unlikely more chemotherapy will be beneficial. If this is the case, then you will receive standard of care chemotherapy and radiation followed by surgery.

At the end of 10-12 cycles of chemotherapy, you will again be evaluated by a surgical oncologist and MRI imaging. If you have had a favorable response and the tumor has resolved, you will not need to have surgery, but you will be periodically evaluated for any recurrence of cancer. If the cancer does progress or return, you may need surgery.

If by the end of 10-12 cycles, your tumor has responded but is not completely gone, you will require radiation and surgery.

During the study, you will have the following assessments:

- You will be asked about your medical history and current medications you are taking.
- You will have physical exams (including vital signs, blood pressure, weight, temperature)
- You will have routine blood work to look at your blood counts, liver and kidney function and your electrolytes. Approximately 1 teaspoon will be taken each time this is drawn.
- You will have routine MRI scans of your pelvis and rectal examinations with

sigmoidoscopy or proctoscopy by a surgical oncologist. You will also have CT scans every 6-12 months per standard of care to make sure the cancer has not spread to any other parts of the body by metastasis.

- All subjects will also complete a quality of life questionnaire at the beginning of the study and then every 3-6 months throughout the duration of the study.

Information about your study participation and study results may be included in your electronic health record. If you have concerns about this or to obtain more detail, you should discuss this with the study team.

Number of Subjects:
Approximately 40 people from multiple sites in the Rochester area will participate in the study.

Duration of the Study:
The treatment portion of this study is expected to last up to 24 weeks. The monitoring portion of the study is expected to last 5 years.

Risks of Participation:
You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. They 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 receiving chemotherapy, but in some cases, they can be serious, long lasting, or may never go away.

Risks and complications related to change in timing of chemotherapy, radiation and surgery:
The study is intended to eliminate the need for surgery. Even if this is not the case, getting chemotherapy first might reduce the tumor prior to surgery, and it might reduce the risk of recurrence. There is a risk with the study that by proceeding to chemotherapy first, if your cancer continues to grow it may be more difficult to remove or treat the tumor with radiation and surgery.

There is also a risk that during surveillance after you have completed treatment, your cancer may return. If this is the case, you will need to be evaluated for surgery and/or radiation treatment. There is a risk that the tumor may return in a place more difficult for surgery, or metastasize to a place where it cannot be surgically resected and become incurable.

The components of the treatments proposed in this study have known side effects that are listed below:

Possible Side Effects of FOLFOX (Leucovorin, 5-Fluorouracil, Oxaliplatin)

COMMON, SOME MAY BE SERIOUS

In 100 people receiving FOLFOX (Leucovorin, 5-Fluorouracil, Oxaliplatin), more than 20 and up to 100 may have:

- Hair loss
- Redness, pain or peeling of palms and soles
- Rash, increased risk of sunburn, itching
- Diarrhea, nausea, vomiting, constipation, loss of appetite
- Difficulty swallowing
- Sores in mouth
- Heartburn
- Infection, especially when white blood cell count is low
- Anemia which may require a blood transfusion
- Bruising, bleeding
- Headache
- Tiredness
- Numbness, tingling or pain, "pins and needles" of the hands, feet, arms and legs
- Tingling or a loss of feeling in your hands, feet, nose, or tightness in throat or jaw, or difficulty swallowing or breathing which may be made worse by exposure to cold
- Cough
- Fever, pain

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving FOLFOX (Leucovorin, 5-Fluorouracil, Oxaliplatin), from 4 to 20 may have:

- Skin changes including dryness, redness or peeling
- Weight gain, weight loss, belly pain
- Changes in taste
- Chest pain
- Abnormal heartbeat which may cause fainting
- Swelling and redness at the site of the medication injection
- Hives
- Blood clot which may cause swelling, pain, shortness of breath
- Liver damage, which may cause yellowing of eyes and skin
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Confusion, dizziness

- Muscle weakness or muscle aches
- Inability to move shoulder or turn head
- Blurred vision, watering eyes
- Discomfort from light
- Abnormal fluid shifts in the body which may cause shortness of breath
- Kidney damage which may require dialysis
- Scarring of the lungs
- Blockage of the airway which may cause shortness of breath, cough, wheezing
- Dehydration
- Abnormal body movement including the eye and eyelid
- Difficulty walking, using your hands, opening mouth, talking, with balance and hearing, smelling, eating, sleeping, emptying the bladder
- Hearing loss

RARE, AND SERIOUS

In 100 people receiving FOLFOX (Leucovorin, 5-Fluorouracil, Oxaliplatin), 3 or fewer may have:

- Damage to the heart, which may cause shortness of breath
- A new cancer resulting from treatment of this cancer
- More severe redness, pain or peeling of palms and soles
- Internal bleeding which may cause black or tarry stool, blood in vomit or urine, or coughing up blood
- Change in voice
- Bleeding from multiple sites including vaginal bleeding, bleeding of the testis, or bleeding of the brain

Possible Side Effects of Short Course Radiation

COMMON, SOME MAY BE SERIOUS

In 100 people receiving short course radiation, more than 20 and up to 100 may have:

- Fatigue
- Diarrhea
- Rectal Pain/Pressure
- Perineal Skin Irritation
- Dysuria

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving short course radiation, from 4 to 20 may have:

- Vomiting
- Abdominal Pain
- Bowel Obstruction
- Fecal Incontinence

Risk of secondary leukemia or other cancers:

In very rare cases, acute leukemia or other cancers may develop after treatment with radiation and the chemotherapy used in this study.

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. The radiation and some of the drugs used in this study may make you unable to have children in the future. For more information about risks and side effects, ask your study doctor. You should expect to use birth control for up to one year after study treatment.

General considerations regarding other risks:

In this study you will undergo periodic CT scans, MRI scans, and evaluation by a surgical oncologist using proctoscopy or sigmoidoscopy.

You will be exposed to radiation from CT scans. The amount of radiation you receive from these diagnostic tests is considered low. The dye injected in your vein during the CT scan may cause pain, burning sensation, hot flushes, and a severe allergic reaction, particularly in those with prior allergies to iodine. CT contrast solution can cause kidney damage, especially if you are diabetic, dehydrated or elderly.

MRI studies do not expose you to radiation. However, they are longer exams than CT scans and may cause anxiety during examination. We can pre-medicate some individuals for this affect. Contrast solution may also be used by IV, with a low risk of allergic reaction, dizziness, headache. However, the contrast solution may need to be held if you have any past kidney injury.

Blood samples will be taken during your clinic visits. The risk of blood drawing includes discomfort at the site of the blood draw with bruising, bleeding, infection and rarely, fainting and nerve damage.

You should always check with your study doctor before you start using any additional treatments during the study.
The study team may be notified if you receive other health care services at URMC or its Affiliates (e.g., visit to the emergency room). In addition, the following individuals may know

you participated in research and may see results of testing conducted for this study:

- Staff at the University of Rochester Medical Center and its Affiliates (e.g., Strong Memorial Hospital, Highland Hospital, URM primary care, specialist physician offices) who have a reason to access your electronic health record.
- Health care providers who are involved in your care at a facility that is not part of the University of Rochester Medical Center and its Affiliates and who have reason to access your electronic health record.
- Individuals who request a copy of information from your health record for activities such as treatment or payment (e.g., medical insurance companies, worker's compensation).

Benefits of Participation

We do not know if you will benefit from this study. You may benefit from not requiring surgery for treatment of your tumor.

New Study Findings

If we discover anything that might make you change your mind about continuing in the study, such as new information from other studies, we will let you know.

Alternatives to Participation

Your other choices may include:

- Getting treatment or care without being in a research study
- Taking part in another research study
- Getting no treatment

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

Costs

Tests and procedures that are required only for the study, that are not a part of your regular medical care, will be provided at no charge.

You or your insurance company will be billed for any standard medical care given during this research study, including the cost of FOLFOX (Leucovorin, 5-Fluorouracil, Oxaliplatin) and its administration. In addition, your insurance company will be billed for the cost of short course radiation. You will be responsible for any co-pays, insurance deductibles and/or co-insurance required by your health insurance carrier for your standard medical care. This standard medical care includes any care that you would receive for the treatment of your type of cancer whether you were participating in a study or not, such as:

- Routine clinic visits with your doctor or nurse practitioner
- Tests (including but not limited to routine items such as: laboratory blood tests, CT, MRI, PET/CT, and/or FDG/PET scans, X-rays, lung function, or cardiac testing.)
- Procedures (including but not limited to routine items such as: bone marrow biopsies and/or aspirates, other tumor biopsies)

- Medications: other standard medications to treat your cancer. This can include other chemotherapies or non-chemotherapy medications used to treat your cancer, and/or medications to treat or prevent side effects.

You may want to talk with your insurance company about its payment policy for standard medical care given during a research study prior to enrolling on a research study. Depending on how your insurance company processes payments for standard medical care given during a research study, you might have unexpected expenses from being in this study. If your insurance company does not pay for your standard medical care, you will be billed for those charges.

Ask your study doctor to discuss the specific costs that will or will not be covered by the sponsor. This discussion should include who will pay the costs of treating possible side effects.

Payments

You will not be paid for participating in this study.

Circumstances for Removal from Study

There are some cases where you could be removed from the study without your consent. You may be withdrawn from the study if your disease does not improve or becomes worse or if your study doctor feels that staying in the study is harmful to your health. You may be withdrawn from the study if you do not keep appointments for study visits, if you experience a treatment delay, or if you cannot complete study activities.

You also may decide that you no longer wish to participate in this research study. If you decide you would like to stop being in this study, we ask that that you notify your study doctor or study coordinator of your decision to stop participation.

Compensation for Injury

If you are directly injured by the drug(s) being studied, or by medical procedures needed because of this study, and you receive medical care for the injury, you may need to pay for that care. You will be reimbursed for reasonable and necessary medical costs for such care, but you might not be reimbursed for care covered and paid for by a third party like your health insurance provider, or costs such as required co-payments or deductibles related to that coverage. No other funds have been set aside to pay for such things as lost wages or expenses due to a current underlying illness or condition.

If your research injury is paid for by the University, we will collect your name, date of birth, gender, and Medicare Health Insurance Claim Number or Social Security Number to determine your Medicare status. This information will be used only in accordance with the law. If you are a Medicare beneficiary, information about the study you are in, and any payments made related to your injury, will be reported to the Centers for Medicare & Medicaid Services (CMS), in accordance with CMS requirements. This information will not be used for any other purpose.

Confidentiality of Records and Authorization to Use and Disclose Information for Research Purposes

The University of Rochester makes every effort to keep the information collected from you private. In order to do so, we will limit access of research information collected on this study to include only trained research personnel assigned to this study. Sometimes, however, researchers need to share information that may identify you with people that work for the University, regulators or the study sponsor.

If you have never received a copy of the University of Rochester Medical Center (URMC) and Affiliates Notice of Privacy Practices, please ask the investigators for one.

What information may be used and given to others?

The study doctor will get your personal and medical information. For example:

- Research records
- Records about phone calls made as part of this research
- Records about your study visits
- Past and present medical records related to this study
- Results of medical tests

Who may use and give out information to you?

- The study doctor and study staff
- URMC and Affiliates

Your information may be given to:

- The University of Rochester, including the Institutional Review Board that oversees the research.
- Other University of Rochester physicians involved in your clinical care.
- Federal and State agencies (such as the U.S. Food and Drug Administration (FDA), the Department of Health and Human Services, the National Institutes of Health and other United States agencies) or government agencies in other countries that oversee or review research. They may also need to inspect study records at some point during the study or even after it has been completed. In the event that this should occur, every effort will be made to keep identifying information about you private.

Why will this information be used and/or given to others?

- To do the research
- To study the results
- To see if the research was done right

If the results of this study are made public, information that identifies you will not be used.

What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study.

May I review or copy my information?
Yes, but only after the research is over.

How long will this permission be valid?
This permission will last indefinitely.

May I cancel my permission to use and disclose information?
Yes. You may cancel your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. Upon receiving the written notice, the study team will no longer use or disclose your health information and you will not be able to stay in this study. Information that has already been gathered may need to be used and given to others for the validity of the study.

May I withdraw from the study?
Yes. If you withdraw your permission to be in the study, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

Is my health information protected after it has been given to others?
No. There is a risk that your information will be given to others without your permission.

More Information
A description of this clinical trial will be available on the internet at http://www.ClinicalTrials.gov as required by U.S. Law. This web site will not include information that can identify you. At most, the web site will include a summary of the results. You can search this web site at any time.

Contact Persons
For more information concerning this research or if you feel that your participation has resulted in any research related injury, emotional or physical discomfort, please contact: Dr. Richard Dunne at 585-275-5863 (24 hours)

Please contact the University of Rochester Research Subjects Review Board at 265 Crittenden Blvd., CU 420628, Rochester, NY 14642, Telephone (585) 276-0005 or (877) 449-4441 for the following reasons:

- You wish to talk to someone other than the research staff about your rights as a research subject;
- To voice concerns about the research;
- To provide input concerning the research process;
- In the event the study staff could not be reached

Voluntary Participation

Participation in this study is voluntary. You are free not to participate or to withdraw at any time, for whatever reason, without risking loss of present or future care you would otherwise expect to receive. In the event that you do withdraw from this study, the information you have already provided will be kept in a confidential manner.

Optional Biomarker Blood Samples

I agree/do not agree that additional blood samples may be collected for use in future health research. Check and initial your choice below.

_____ (initials) Agree _____ (initials) Do not Agree

Signature/Dates

After reading and discussing the information in this consent form you should understand:

- Why this study is being done;
- What will happen during the study;
- Any possible risks and benefits to you;
- Other options you may have instead of being in the study;
- How your personal information will be protected;
- What to do if you have problems or questions about this study

Subject Consent

I have read (or have had read to me) the contents of this consent form and have been encouraged to ask questions. I have received answers to my questions. I agree to participate in this study. I will receive (or will receive) a signed copy of this form for my records and future reference.

_____

Subject Name (Printed by Subject)

_____ _____

Signature of Subject Date

Person Obtaining Consent

I have read this form to the subject and/or the subject has read this form. I will provide the subject with a signed copy of this consent form for their records and future reference. An explanation of the research was given and questions from the subject were solicited and answered to the subject's satisfaction. In my judgment, the subject has demonstrated comprehension of the information. I have given the subject adequate opportunity to read consent before signing.

_____ _____

Name of Person Obtaining Consent (Print) Date

_____

Signature of Person Obtaining Consent