THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

A Phase Ib Trial of Preoperative Short-Course Chemoradiotherapy followed by Chemotherapy for Resectable Gastric and Gastroesophageal Adenocarcinoma
2020-0481

Study Chair: Brian Badgwell

_____ _____
Participant's Name Medical Record Number

This is an informed consent and authorization form for a research study. It includes a summary about the study. A more detailed description of procedures and risks is provided after the summary.

STUDY SUMMARY

The goal of this clinical research study is to learn if a shorter course of chemo-radiotherapy (chemotherapy and radiation treatment for 2 weeks instead of 5 weeks) followed by standard chemotherapy may be more effective in treating patients with gastric and gastroesophageal cancer who are scheduled to have treatment and then surgery to remove the tumor. Researchers also want to learn if a shorter course of radiation affects tumor surgery success. The safety of this combination treatment will be studied.

This is an investigational study. The chemotherapy being given in this study is FDA approved and commercially available. The study doctor can explain how the study drug(s) are designed to work. Radiation therapy is delivered using FDA-approved and commercially available methods, and in combination with low-dose chemotherapy. The investigational part of this study is that the course of treatment is shorter.

Receiving short-course chemo-radiotherapy before chemotherapy and surgery may help to control the disease. Future patients may benefit from what is learned in this study. There may be no benefits for you in this study.

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects, potential expenses, and time commitment. If you take part in this study, you may experience side effects, some of which may be severe or fatal.

You can read a full list of potential side effects below in the Possible Risks section of this consent.

Your participation may last for at least 20 weeks before your surgery. After surgery, you will have imaging scans done every 6 months for up to 5 years. Imaging scans may be completed outside of MD Anderson if needed, and the study staff will request records of those results.

You and/or your insurance company will be responsible for the cost of treatment and surgery.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive standard-of-care treatment for the disease, including other methods of receiving chemo-radiotherapy, surgery, or chemotherapy alone. You may choose to receive other investigational therapy, if available. You may choose not to have treatment for cancer at all. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

1. STUDY DETAILS

Screening Tests

Signing this consent form does not mean that you will be able to take part in this study. The following screening tests will help the doctor decide if you are eligible:

- You will have a physical exam.
- Blood (about 2-3 tablespoons) will be drawn for routine tests. If you can become pregnant, part of this blood sample or urine will be collected for a pregnancy test. To take part in this study, you must not be pregnant.
- If you have not had them done in the last 8 weeks, imaging scans (CT, MRI, or PET/CT scans) of the chest, abdomen, and/or pelvis will be collected to check the status of the disease.

The study doctor will discuss the screening test results with you. If the screening tests show that you are not eligible to take part in the study, you will not be enrolled. Other treatment options will be discussed with you.

Up to 24 participants will take part in this research study. All will be enrolled at MD Anderson.

Study Treatment and Drug Administration

Chemo-Radiation Treatment

If you are found to be eligible to take part in this study, you will receive radiation therapy 5 days a week (Monday through Friday) for 2 weeks. Along with this radiation schedule, you will receive standard-of-care chemotherapy (either capecitabine or fluorouracil [5-FU]):

- **Capecitabine** will be taken by mouth 2 times a day, on Monday through Friday of each radiation treatment week.
- **Fluorouracil** is given by vein continuously (non-stop) Monday through Friday of each radiation week.

Your doctor will let you know which chemotherapy drug you will receive.

Pre-Surgery Chemotherapy
After receiving chemoradiation, you will begin receiving standard-of-care chemotherapy for up to 2 months before surgery. The type of chemotherapy you receive will depend on what the doctor thinks is in your best interest. The study doctor will tell you which therapy you will receive and how often you will receive it. You will be given a standard consent form for this treatment, which will also explain its risks.

You will then have a break from treatment that will last about 4-6 weeks, followed by restaging (testing to see how the cancer has responded to treatment) and surgery.

Surgery
After the treatment break and restaging tests, you will have surgery to remove the tumor as part of your standard care. You will be given a standard surgical consent to sign, which will explain the surgery and its risks in more detail.

Study Tests

Each week during chemo-radiation, blood (about 2-3 tablespoons) will be drawn for routine tests.

About 4 weeks after finishing pre-surgery chemotherapy, you will have a restaging visit. At this visit:

- You will have a physical exam.
- Blood (about 2-3 tablespoons) will be drawn for routine tests.
- Imaging scans (CT, MRI, or PET/CT scans) of the chest, abdomen, and/or pelvis will be collected to check the status of the disease.

At the time of your surgery, you will have a physical exam.

Follow-up

About every 6 months after surgery for up to 5 years, you will be contacted by phone, email, or in-person and asked about your health status. Imaging scans may also be collected as part of follow-up, but this is not required.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. You should discuss these with the study doctor. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after treatment is stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Side effects will vary from person to person, and some may occur after you have stopped receiving treatment. Tell the study staff about any side effects you may have, even if you do not think they are related to the study drugs/procedures.

Fluorouracil and capecitabine each may cause low blood cell counts (red blood cells, platelets, and/or white blood cells):

- A low red blood cell count (anemia) may cause difficulty breathing and/or fatigue. You may need a blood transfusion.
- A low platelet count increases your risk of bleeding (such as nosebleeds, bruising, stroke, and/or digestive system bleeding). You may need a platelet transfusion.
- A low white blood cell count increases your risk of infection (such as pneumonia and/or severe blood infection). Infections may occur anywhere and become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

Radiation Therapy Side Effects

It is not known how often the side effects of radiation therapy may occur.

• swelling • swelling of the arms or torso • skin changes (possible dryness, itching, peeling, and/or blistering)	• hair loss at the treatment site • mouth problems • trouble swallowing • nausea • vomiting • diarrhea	• urinary and/or bladder changes • sexual changes • inability to produce children • joint problems • secondary cancers

Radiation therapy may cause you to develop another type of cancer. Side effects may not occur for up to 6 months after radiation therapy is over. Side effects will vary depending on what part of the body is receiving radiation therapy.

Fluorouracil Side Effects

It is not known how often the side effects of fluorouracil may occur.

• chest pain due to heart trouble • irregular heartbeat • heart failure • heart attack • decreased blood supply to the heart • blood vessel spasm (possible blockage of blood flow) • blood clots in a vein at the injection site (possible pain, swelling, and/or redness) • abnormal brain function (affecting balance and coordination) • confusion • euphoria (unusual feelings of happiness or well-being) • headache • stroke • hair loss (partial or total)	• skin rash • darkening of the skin • dry and/or peeling skin • skin sores • hand-foot syndrome (palms of hands/soles of feet having pain, swelling, and blistering) syndrome • skin sensitivity to sunlight or lamps • very severe blistering skin disease (with ulcers of the skin and digestive tract) • very severe blistering skin disease (loss of large portion of skin) • nail changes (possible nail loss) • swollen throat • abnormal taste • mouth blisters/sores (possible difficulty swallowing)	• digestive system bleeding • stomach and/or small intestine ulcer • loss of appetite • diarrhea • vomiting /nausea • decreased supply of blood to the abdomen • low blood counts (red, white, platelets) • eye sensitivity to light • vision problems • eye twitching • teary eyes (possibly due to narrowing of the tear ducts) • nosebleed • allergic reaction that may be life-threatening (such as difficulty breathing, low blood pressure, and/or organ failure)

<u>Capecitabine Side Effects</u>

Common (occurring in more than 20% of patients)

• fatigue • hand-foot syndrome (palms of hands/soles of feet having pain, swelling, and blistering, with possible distorted fingerprints) • skin rash • loss of appetite	• mouth blisters/sores (possible difficulty swallowing) • diarrhea • nausea • vomiting • abdominal pain • low blood counts (red, white, platelets)	• abnormal liver tests (possible liver damage and/or yellowing of the skin and/or eyes) • abnormal sensation (such as pins and needles) • weakness

Occasional (occurring in 5-20% of patients)

• chest pain (possibly due to heart trouble) • blood clots in a vein (possible pain, swelling, and/or redness) • swelling • fever • headache • dizziness • difficulty sleeping • mood swings	• depression • nail changes • change of skin color • hair loss (partial or total) • dehydration • abnormal taste • mouth pain • upset stomach • constipation • intestinal blockage • pain	• nerve damage (loss of motor or sensory function) • painful red eyes • eye irritation • vision problems • cough • difficulty breathing (possibly due to narrowing of the airways) • infection

Exact frequency unknown but occurring in 1-10% of patients

• sudden stopping of the heart • enlarged heart • heart attack/failure	• decreased blood supply to the heart • irregular heartbeat • abnormal EKG	• inflammation of the intestine and decreased blood flow to part of the bowel (possible tissue death)

Frequency unknown but occurring in fewer than 5% of patients

• irregular/slow heartbeat • extra heartbeats • build-up of fluid in the tissue around the heart • hot flashes • lymphedema (swelling of arms/legs/torso) • sedation • difficulty forming or speaking words • itching • skin sores	• abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood pressure, organ failure, heart problems, changes in mental status, and/or seizure) • weight gain • enlarged bowel (possible abdominal pain) • inflammation of the stomach and/or intestines	• abdominal swelling • coughing up blood • difficulty walking • tremors • eye inflammation • flu-like symptoms • nosebleed • inflammation of the voice box • difficulty swallowing • throat inflammation • thirst • hoarseness • allergic reaction

Rare but serious (occurring in fewer than 3% of patients)

• fast heartbeat • high blood pressure • low blood pressure • (possible dizziness/fainting) • heart inflammation • abnormal blood clotting • stroke • fainting • loss of consciousness • decreased brain function (possible paralysis and/or coma) • very severe blistering skin disease (with ulcers of the skin and digestive tract)	• very severe blistering skin disease (loss of large portion of skin) • severe sunburn-like rash at site of previous radiation (called radiation recall) • high blood levels of fat (possible heart disease and/or stroke) • severe weight loss • fluid in the abdomen • hole in the intestines (possibly leaking contents into the abdomen) • stomach ulcer • lupus (an immune system disease)	• inflammation of the bile tract (possible blockage) • liver damage/failure • scarring of the liver • jaundice (yellowing of skin and/or eyes) • narrowing of the tear ducts (possible teary eyes) • kidney failure • blockage in the lung (possible pain and/or shortness of breath) • lung inflammation • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)

Capecitabine may cause sudden death. It is not known how often this may occur.

Capecitabine may increase the blood-thinning effects of warfarin. Combining capecitabine with warfarin may cause bleeding and/or death.

Using the study drugs and radiation together may cause side effects that are not seen when each is given alone. The study drug combination may also increase the frequency and/or severity of the side effects listed above.

Other Risks

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

During the **MRI**, you may feel mild vibrations throughout your body. The machine will produce a loud knocking noise. This is normal. You will be given earplugs to protect your ears. Some people, especially those who tend to feel uncomfortable in small or closed spaces, may feel “closed in” and become anxious while in the scanner. The scanner has an intercom, which will allow you to speak to the staff during the procedure. If you feel ill or anxious during scanning, tell the MRI staff and the scanning will be stopped if you wish. The MRI will require a catheter to be inserted into one of your veins in order to inject the MRI contrast agent. This may cause skin

irritation, bleeding, and/or infection. You may have an allergic reaction to the contrast agent.

The magnetic field used in MRI scanning may harm you if you have certain types of metal in your body (as might be found in pacemakers, neurostimulators, or certain clips). It may cause problems with devices, such as pacemakers. If you have metal in your body or devices such as a pacemaker, you should discuss this with the study doctor.

CT and PET-CT scans send x-rays through the body at many different angles. You will be exposed to a small dose of radiation. All radiation adds up over a lifetime and may increase the risk of new cancer forming. Some people may feel "closed in" while lying in the scanner. However, the scanner is open at both ends, and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or radiology technicians will give comfort, or the scanning will be stopped. Solution may also be given by vein to make the x-ray pictures more accurate. This may cause an uncomfortable feeling of warmth, nausea, and/or severe allergic reactions. The solution injection may also cause pain, bleeding, bruising, hives, and/or itching.

This study may involve unpredictable risks to the participants.

Pregnancy Related Risks

Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant, breastfeed a baby, or father a child while on this study. You must use birth control while you are receiving study treatment, if you are sexually active.

Birth Control Specifications: Acceptable methods of birth control include any of the following:

- Hormonal birth control (oral ["the pill"], injectable)
- Intrauterine devices (IUDs)
- Double-barrier methods (use of a condom with spermicide) – Males must use condoms.

Please let the study doctor know which method(s) of birth control you plan to use.

Males: Tell the doctor right away if your partner becomes pregnant or suspects pregnancy.

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away.

Getting pregnant will result in your removal from this study.

3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson for this injury. You may also contact the Chair of MD Anderson's IRB at 713-792-6477 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

Certain tests, procedures, and/or drugs that you may receive as part of this study may be without cost to you because they are for research purposes only. However, your insurance provider and/or you may be financially responsible for the cost of care and treatment of any complications resulting from the research tests, procedures, and/or drugs. Standard medical care that you receive under this research study will be billed to your insurance provider and/or you in the ordinary manner. Before taking part in this study, you may ask about which parts of the research-related care may be provided without charge, which costs your insurance provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this study.

Samples that are collected from you in this study may be used for the development of treatments, devices, new drugs, or patentable procedures that may result in commercial profit.

There are no plans to compensate you for any patents or discoveries that may result from your participation in this research.

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

Additional Information

4. You may ask the study chair (Dr. Brian Badgwell, at 713-745-7351) any questions you have about this study. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-6477 with any questions that have to do with this study or your rights as a study participant.

5. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor. If you withdraw from this study, you can still choose to be treated at MD Anderson.

   Your personal information is being collected and is a mandatory part of this study. If you choose to leave the study early for any reason, the study team will document your decision in your medical chart. The study team may ask you to allow information from your medical record and the results of your routine medical care to keep being collected for this research study.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson.

7. You will be informed of any new findings or information that might affect your willingness to continue taking part in the study, and you may be asked to sign another informed consent and authorization form stating your continued willingness to participate in this study.

8. MD Anderson may benefit from your participation and/or what is learned in this study.

Future Research

Data

Your personal information is being collected as part of this study. These data may be used by researchers at MD Anderson and/or shared with other researchers and/or institutions for use in future research.

Before being used or shared for future research, every effort will be made to remove your identifying information from any data. If all identifying information is removed, you will not be asked for additional permission before future research is performed.

In some cases, all of your identifying information may not be removed before your data are used for future research. If future research is performed at MD Anderson, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson before your data can be used. At that time, the IRB will decide whether or not further permission from you is required. The IRB is a committee of doctors, researchers, and community members that is responsible for protecting study participants and making sure all research is safe and ethical.

If this research is not performed at MD Anderson, MD Anderson will not have oversight of any data.

You may withdraw your consent to future research at any time. If you do not want your data to be used for future research, tell the study doctor.

Outside Care

Part of your care may be provided outside of MD Anderson by your home doctor(s). Follow-up imaging may be completed at an outside facility as needed.

Authorization for Use and Disclosure of Protected Health Information (PHI):

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:
   - Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
   - The IRB and officials of MD Anderson
   - Study monitors and auditors who verify the accuracy of the information
   - Individuals who put all the study information together in report form

B. Signing this consent and authorization form is optional but you cannot take part in this study or receive study-related treatment if you do not agree and sign.

C. MD Anderson will keep your PHI confidential when possible (according to state and federal law). However, in some situations, the FDA could be required to reveal the names of participants.

   Once disclosed outside of MD Anderson, federal privacy laws may no longer protect your PHI.

D. The permission to use your PHI will continue indefinitely unless you withdraw your authorization in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP) or you may contact the Chief Privacy Officer at 713-745-6636. If you withdraw your authorization, you will be removed from the study and the data collected about you up to that point can be used and included in data analysis. However, no further information about you will be collected.

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

CONSENT/AUTHORIZATION

I understand the information in this consent form. I have had a chance to read the consent form for this study or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under Protocol 2020-0481.

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE

A witness signature is only required for vulnerable adult participants. If witnessing the assent of a pediatric participant, leave this line blank and sign on the witness to assent page instead.

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

PERSON OBTAINING CONSENT

I have discussed this research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT

TRANSLATOR

I have translated the above informed consent as written (without additions or subtractions) into_____and assisted the people
(Name of Language)
obtaining and providing consent by translating all questions and responses during the consent process for this participant.

_____ _____ _____
NAME OF TRANSLATOR SIGNATURE OF TRANSLATOR DATE

☐ Please check here if the translator was a member of the research team. (If checked, a witness, other than the translator, must sign the witness line below.)

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL TRANSLATION DATE
(OTHER THAN TRANSLATOR, PARENT/GUARDIAN,
OR STUDY CHAIR)

_____
PRINTED NAME OF WITNESS TO THE VERBAL TRANSLATION