THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

Phase II Trial of 5-FU, Leucovorin, Gemcitabine, and Cisplatin for Adenocarcinomas of the Urothelial Tract and Urachal Remnant ID03-0111

Study Chair: Arlene Siefker-Radtke

1. _____ _____
Participant's Name Medical Record Number

You are being asked to take part in this clinical research study at The University of Texas M. D. Anderson Cancer Center ("M. D. Anderson"). This consent form explains why this research study is being done and what your role will be if you choose to take part. This form also describes the possible risks connected with being in this study. After reviewing this information with the person responsible for your enrollment, you should know enough to be able to make an informed decision on whether you want to take part in the study.

You are being asked to take part in this study because you have adenocarcinoma, a type of bladder cancer.

DESCRIPTION OF RESEARCH

2. PURPOSE OF STUDY

The goal of this clinical research study is to learn if treatment with a combination of 4 chemotherapy drugs can help to shrink or slow the growth of adenocarcinoma. The drugs used in the combination chemotherapy are: 5-fluorouracil (5FU), leucovorin, gemcitabine, and cisplatin.

3. DESCRIPTION OF STUDY

Adenocarcinoma is an uncommon tumor of the bladder and urinary tract. Because this tumor is so rare, there is no current standard treatment for the disease. For this study, researchers will study the effects of a 4-drug combination of chemotherapy in the treatment of adenocarcinoma. The 4 chemotherapy drugs being used in this study are all commonly used to treat other types of cancer.

Before treatment starts, you will have a complete physical exam. You will have blood (2-3 tablespoons) and urine samples collected for routine lab tests and for tests to evaluate bone marrow, liver, and kidney functions. You will have a chest x-ray and an electrocardiogram (ECG – a test that measures the electrical activity of the heart). You will also have CT scans of the chest, abdomen (stomach), and pelvis (waist area), as well as a bone scan (x-rays of your bones). These tests are being done to check the size and location of the tumor(s). If your doctor feels it is necessary, you may have a MRI of the brain. Women who are able to have children must have a negative blood or urine pregnancy test. All of these tests are part of the standard care for the disease.

For this study, you will receive 4 chemotherapy agents. You will be admitted to the hospital for around 5 days each time you receive treatment. Treatments will be repeated every 21 days. Each 21-day period is called one “cycle” of therapy. Treatment with the drugs will be given through a catheter (small flexible tube) placed in a large vein in the chest or arm. The drugs will be given to you through this catheter over several days. This method of giving drugs is called an infusion.

5FU will be given as a continuous infusion over Days 1 through 5. Leucovorin will be given once a day as a short infusion on Days 1 through 5. Cisplatin will be given by infusion over a few hours (usually 2-4 hours) once a day on Days 1 through 5. Gemcitabine will be given by infusion over 30 minutes on Days 1 and 5 only.

The cycles will be repeated as long as the tumor is not growing and there are no severe side effects. There is no set limit on the number of cycles you will receive. However, most participants can expect to receive between 2 and 6 cycles of therapy (6-18 weeks).

During treatment, you will have frequent (every other day beginning around Day 9) blood tests (2-3 tablespoons) to measure bone marrow function. A physical exam and blood tests (2-3 tablespoons) will be repeated before starting each cycle of treatment. Based on the results of these blood tests, you may need treatment with injections of a drug called G-CSF to increase your white blood cell counts.

You will be asked to return to UTMDACC every 6 weeks for a physical exam and blood tests (2-3 tablespoons) to evaluate liver, kidneys, bone marrow, and electrolytes. Every 6 weeks, you will also have tests to evaluate the areas involved by cancer. This usually includes a CT-scan, and/or chest x-ray depending on the

location of the disease.

Participants will be on study as long as the tumor is not growing and there are not severe side effects. Therapy may be stopped and participants will be taken off study early if one or both of these things occur. While there is not set limit on the total number of cycles of chemotherapy you may receive, most patients will receive between 2 and 6 cycles, or approximately 6-18 weeks of therapy. If, at any time, the disease gets worse or you experience any intolerable side effects, you will be taken off the study and your doctor will discuss other treatment options with you.

After your last treatment, you will have long-term follow-up visits scheduled at the Center for GU Oncology, usually around every 3-6 months. These visits usually include blood tests (2-3 tablespoons) a CT scan, and/or chest x-ray depending on the location of the disease.

This is an investigational study. All of the chemotherapy drugs used in this study are FDA approved and commercially available. Up to 46 participants will take part in this study. All will be enrolled at UTMDACC.

4. RISKS, SIDE EFFECTS, AND DISCOMFORTS TO PARTICIPANTS

While on this study, you are at risk for side effects. These side effects will vary from person to person. The more commonly occurring side effects are listed in this form, as are rare but serious side effects that the drug is known to cause. You should discuss these with the study doctor. 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 cause death.

Placement of a **central venous line (CVL)** may cause infection and/or clotting of the central vein or the central line. Treatment of central line infection typically includes antibiotics and may require removal of the infected central line and placement of another central venous line. Pain, redness, swelling, bruising, and/or vein irritation may occur where the CVL enters the body. Clotting of the central vein or central line is treated with medications and may require removal of the central line. Placement of a central venous line may cause a puncture of the axillary artery (with swelling and/or bruising) and/or pneumothorax (air around the lung). Treatment of puncture of the axillary artery generally includes application of pressure at the site of the bleeding. Treatment of pneumothorax generally includes observation, aspiration (suctioning out the air), or insertion of a tube into the chest to remove the air. Placement of a central venous line may also cause central line migration (movement) or breakage of the central line. You will have to sign a separate consent document before placement of a CVL can be performed.

5-fluorouracil Side Effects (IV)
It is not known how often the side effects of 5-fluorouracil occur

● chest pain due to heart trouble ● decreased blood supply to the heart ● nail changes ● trouble with balance ● confusion ● euphoria (unusual feelings of great happiness or well-being) ● headache ● eye movement disorder ● hair loss ● skin inflammation	● dry skin ● skin breakage ● sores ● hand-foot syndrome (pain, swelling, blistering, and/or redness of the hands and/or feet) ● nail loss ● shedding of skin ● itchy skin rash ● skin sensitivity to light ● darkened vein color ● loss of appetite ● diarrhea ● nausea	● swelling deep in the throat ● sores in the mouth ● vomiting ● bleeding ● inflammation of a vein caused by blood clot ● teary eyes ● narrowing of the tear ducts that drain the eyes ● eye sensitivity to light ● vision changes ● nosebleeds ● allergic reaction

5-fluorouracil may cause low blood cell counts (white blood cells, red blood cells, and platelets). This means that while you take the drug, there is more of a chance of getting an infection, including pneumonia. You may become anemic and/or have problems with bleeding, bruising, fatigue, and/or shortness of breath. You may need a blood transfusion.

Gemcitabine Side Effects
Likely (occurring in more than 20% of patients)

● pain ● fever ● skin rash ● nausea ● vomiting ● constipation	● diarrhea ● abnormal liver tests (possible liver damage) ● jaundice (yellowing and/or darkening of skin)	● increased proteins in the urine (possible kidney damage) ● blood in the urine ● difficulty breathing

Gemcitabine hydrochloride may likely cause low blood cell counts (white blood cells, red blood cells, and platelets). This means that while you take the drug, there is more of a chance of getting an infection, including pneumonia. You may become anemic and/or have problems with bleeding, bruising, fatigue, and/or shortness of breath. You may need a blood transfusion.

Common (occurring in 3-20% of patients)

● arm and/or leg swelling ● swelling	● abnormal kidney test (possible decreased	● bleeding ● tickling/tingling

● drowsiness ● hair loss ● itching ● sores in the mouth	kidney function) ● increased creatinine blood level (possible kidney problems)	sensation ● flu-like symptoms ● infection ● injection site reactions

Rare but serious (occurring in 3% or fewer patients)

● irregular heartbeat ● heart failure ● heart attack ● high blood pressure ● stroke ● chills ● headache ● rash that is like a severe sunburn (radiation recall) ● decay of body tissue ● loss of appetite ● liver failure	● liver damage ● inflammation in blood vessels (possible fever and/or fatigue) ● destruction of red blood cells ● blood infection ● kidney failure ● weakness ● lung inflammation ● tightening of the airways	● lung injury causing severe shortness of breath ● build-up of fluid in the lungs ● scarring of the lung ● abnormal level of oxygen and carbon dioxide in the blood ● inflammation in the nose ● severe allergic reactions

Cisplatin Side Effects

Likely (occurring in more than 20% of patients)

● nausea	● vomiting	● hair loss

Cisplatin may likely cause ear damage, such as ringing in the ears, loss of high frequency hearing, and/or deafness. There is a higher chance of this side effect occurring in children.

Cisplatin may likely cause low blood cell counts (white blood cells, red blood cells, and platelets). This means that while you take the drug, there is more of a chance of getting an infection, including pneumonia. You may become anemic and/or have problems with bleeding, bruising, fatigue, and/or shortness of breath. You may need a blood transfusion.

Common (occurring in 3-20% of patients)

● pain or weakness ● nervous system damage	● abnormal liver function tests, which could mean liver damage	● diarrhea ● kidney damage ● tissue irritation

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

● irregular/slow heartbeat ● low blood pressure ● destruction of red blood cells	● inflammation of the veins, which can lead to blood clots ● severe kidney damage or failure	● hormone changes related to kidney function ● allergic reaction ● swelling of the optic nerve

Leucovorin Side Effects

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

● rash ● itching ● skin redness ● hives	● increased blood platelet count (possible blood clotting problems)	● wheezing ● allergic reaction, possibly severe

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. When a CT scan of the abdominal area is taken, material may be inserted into the rectum to better define the bowel. You will usually drink liquid to help define various abdominal organs. This may cause nausea and/or vomiting. Solution may also be given by vein to make the x-ray pictures more accurate. This may cause flushing, nausea, and/or severe allergic reactions. The solution injection may also cause pain, bleeding, bruising, hives, and/or itching.

MRI (magnetic resonance imaging) uses a large magnet instead of x-rays to take pictures of the inside of your body. People who have metal in their bodies (pacemakers, neurostimulators, certain clips, or staples from prior surgery) may not receive an MRI. The magnetic field used in MRI scanning may harm such people or cause problems with devices such as pacemakers. Part or all of the body will be passed into a long, narrow tube scanner, which is open at both ends. The scanner has an intercom, which will allow you to speak to the doctors and staff during the procedure. The machine will produce a loud knocking noise. This is normal. You will be given earplugs to protect your ears. In addition, you may feel light vibrations throughout your body. Some people, especially those who have a tendency to feel uncomfortable in small or closed spaces, may feel "closed in" and become anxious while in the scanner. If you feel ill or anxious during scanning, doctors and the MRI staff will give comfort or the scanning will be stopped. The MRI will require a line to be inserted into one of your veins to inject the MRI contrast agent. This may cause local irritation, bleeding, and/or infection. You may have an allergic reaction to the contrast agent.

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.

This study may involve unpredictable risks to the participants.

Pregnancy Related Risks

4a. Because taking part in this study can result in risks to an unborn or breastfeeding baby, you should not become pregnant, breastfeed a baby, or father a child while on this study. You must use birth control during the study if you are sexually active.

Birth Control Specifications: Men and women of childbearing potential must use acceptable methods of birth control (such as birth control pills, condoms, approved contraceptive implant, intrauterine device, or tubal ligation) throughout the study to prevent pregnancy. If you are pregnant, you may not be enrolled on this study. Mothers should not breast-feed during the study.
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 may result in your removal from this study.

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

5. POTENTIAL BENEFITS

Treatment on this study may help to shrink or slow the growth of the cancer. There may be no benefits for you in this study. There may be no benefits for you in this study.

6. ALTERNATE PROCEDURES OR TREATMENTS

You may choose not to take part in this study. You may choose not to take part in this study. 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.

I understand that the following statements about this study are true:

7. M. D. Anderson may benefit financially from my participation and/or from what is learned in this study.

8. This study is supported by: the Charlene Curlee Fund.

9. I may ask the study chair any questions I have about this study, including questions about the costs. I may contact the study chair, Dr. Arlene Siefker-Radtke, at 713-792-2830. I may also contact the Chair of M. D. Anderson's IRB at 713-792-2933 with any questions that have to do with this study or my rights as a study participant.

10. My participation in this research study is strictly voluntary. I may refuse to take part in this study without any penalty or loss of benefits to which I am otherwise entitled. I may also withdraw from participation in this study at any time without any penalty or loss of benefits. I should first discuss leaving the study with my doctor. If I withdraw from this study, I may still be treated at M. D. Anderson.

11. I understand that the study may be changed or stopped at any time by the study chair, the Charlene Curlee Fund, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP) (a regulatory agency that oversees research in humans), or the IRB of M. D. Anderson.

12. I will be informed of any new findings that might affect my willingness to continue taking part in the study.

13. M. D. Anderson will take appropriate steps to keep my personal health information private. However, there is no guarantee of absolute privacy. Federal agencies (such as the FDA and the OHRP), the Charlene Curlee Fund, and the IRB of M. D. Anderson might review my record to collect data or to check that the research is being done safely and correctly. In some situations, the FDA could be required to reveal the names of participants.

14. If I suffer injury as a direct result of taking part in this study, M. D. Anderson will provide medical care. However, this medical care will be billed to my insurance provider or me in the ordinary manner. I understand that I will not be reimbursed for expenses or compensated financially by M. D. Anderson or the Charlene Curlee Fund for this injury. I may also contact the Chair of M. D. Anderson’s IRB at 713-792-2933 with questions about study-related injuries.

15. Certain tests, procedures, and/or medications that I may receive as part of this study may be without cost to me because they are for research purposes only. However, my insurance provider or I may be financially responsible for the cost of supportive care and treatment of any complications resulting from the research tests, procedures, and/or medications, including hospitalization, nausea, vomiting, low blood cell counts, and dehydration. Standard medical care that I receive under this research study will be billed to my insurance provider and/or me in the ordinary

manner. I should learn before taking part in this study which parts of the research-related care will be provided without charge, which costs my insurance provider will pay for, and which costs will be my responsibility. I may ask to speak with a financial counselor about the costs of this study.

16. I understand that there are no plans to compensate me for any patents or discoveries that may result from my participation in this research. I will receive no compensation for taking part in this study.

Authorization for Use and Disclosure of Protected Health Information:

A. During the course of this study, the research team at M. D. Anderson will be collecting information about you. This information may include your medical history, study schedule, and the results of any of your tests, therapies, and/or procedures. The purpose of collecting and sharing this information is to learn about how the study procedures may affect the disease and any study-related side effects. Your doctor and the research team may share your study information with the parties named in Section E below.

B. If you refuse to provide your authorization to disclose your protected health information, you will not be able to participate in this research study.

C. Your protected health information will be protected according to state and federal law. However, there is no guarantee that your information will remain confidential, and it may be re-disclosed at some point.

D. All identifying information such as your name and address will be kept private. This information may be kept at M. D. Anderson forever. You will be assigned a code number so that your name will not be used. The research team at M. D. Anderson will be able to link the code number to your name. In some instances, in order to ensure the scientific value of the study, the parties named in Section E below will be able to view your study record but will not be permitted to copy any identifying information contained in your record.

E. Your information may be shared with the following parties:

- the Charlene Curlee Fund
- The FDA
- The OHRP
- The IRB of M. D. Anderson
- Officials of M. D. Anderson
- Clinical study monitors who verify the accuracy of the information
- Individuals with medical backgrounds who determine the effect that the study procedures may have on the disease
- Individuals who put all the study information together in report form

F. You have the right to see and reproduce your records related to the research study, and ask for corrections, for as long as this information is held by the study chair and/or M. D. Anderson. However, in some studies, in order to ensure the scientific value of the study, participants are not able to view or reproduce their study records until the research has been completed with all participants in the study. If possible for this study, your doctor will be able to discuss your clinical test results with you.

G. There is no expiration date for the use of your protected health information. You may withdraw your authorization to share your protected health information at any time in writing. Instructions on how to do this can be found in the M. D. Anderson Notice of Privacy Practices (NPP). You may contact the IRB Staff at 713-792-2933 with questions about how to find the NPP. If you withdraw your authorization, you will be removed from the study and the study chair and staff will no longer use or disclose your protected health information in connection with this study, unless the study chair or staff needs to use or disclose some of your research-related protected health information to preserve the scientific value of the study. The parties listed in Section E above may use any study data that were collected before you canceled your authorization.

H. Information about this research study may be submitted to ClinicalTrials.gov, a publicly available online database managed by the U. S. National Institutes of Health. None of your identifying information will be submitted to ClinicalTrials.gov. If information from this study is submitted, none of it will be able to be directly linked to you.

CONSENT/PERMISSION/AUTHORIZATION FOR TREATMENT

Having read and understood the above and having had the chance to ask questions about this study, think about the study, and talk 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 have been given a signed copy of this consent document.

SAMPLE -- NOT FOR USE IN CONSENTING PATIENTS

SIGNATURE OF PARTICIPANT DATE

I was present during the explanation of the research to be performed under Protocol **ID03-0111**.

SAMPLE -- NOT FOR USE IN CONSENTING PATIENTS

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

SAMPLE -- NOT FOR USE IN CONSENTING PATIENTS

SIGNATURE OF PERSON RESPONSIBLE & RELATIONSHIP DATE

I have discussed this clinical 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.

SAMPLE -- NOT FOR USE IN CONSENTING PATIENTS

SIGNATURE OF STUDY CHAIR OR PERSON OBTAINING CONSENT DATE

Translator

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

SAMPLE -- NOT FOR USE IN CONSENTING PATIENTS

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.)