Informed Consent Form

Clinical Trials.gov number: NCT02775695

Protocol Title: Efficacy of doxycycline on metakaryote cell death in patients with resectable pancreatic cancer

Document Date: 02/14/2018

Medical College of Wisconsin and Froedtert Hospital
CONSENT TO PARTICIPATE IN RESEARCH

Name of Study Subject: _____

Efficacy of doxycycline on metakaryote cell death in patients with resectable pancreatic cancer

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You are invited to take part in this research study. This form tells you why this research study is being done, what will happen in the research study, possible risks and benefits to you, your choices, and other important information. If there is anything that you do not understand, please ask questions. Then you can decide if you want to join this study or not.

A1. INTRODUCTION – WHY ARE WE ASKING YOU ABOUT THIS STUDY?

You are being invited to participate in this research study because you have been diagnosed with pancreatic cancer that can be removed surgically. You may be eligible for a research study assessing the effectiveness of the drug “doxycycline” to treat pancreatic cancer. Doxycycline is an FDA-approved antibiotic that is being evaluated for its ability to kill certain cancer stem cells.

A total of about 12 people are expected to participate in this study at Froedtert Hospital/Medical College of Wisconsin.

The Director of the study is Susan Tsai, MD, MHS in the Division of Surgical Oncology. A study team works with Dr. Tsai. You can ask who these people are. This study is funded by the Batterman Foundation.

A2. DO I HAVE TO BE IN THIS STUDY?

You can decide whether to take part in this study or not. You are free to say yes or no. If you say no, your regular medical care will not change. Even if you join this study, you do not have to stay in it. You may stop at any time.

A research study is different from routine medical care in three ways: 1) there are extra risks that we will tell you about in this form; 2) you may have some extra medical tests and visits; 3) the study procedures, tests and visits follow a set plan that must be kept.

A3. WHY IS THIS RESEARCH STUDY BEING DONE?

The purpose of this study is to evaluate the effectiveness of using doxycycline to kill cancer stem cells (metakaryotic cells) in pancreatic tumors from patients with pancreatic tumors that can be removed surgically.

Everyone in this study will receive doxycycline which is approved by the U.S. Food and Drug Administration for use in patients but for other purposes. We don't know if this study will help you. Your condition may get better but it could stay the same or even get worse. You may or may not benefit from participating in this trial. We hope the information from this study will help us develop a better treatment for pancreatic cancer in the future.

B1. WHAT WILL HAPPEN IF I TAKE PART IN THE STUDY?

Screening procedures:

If you decide to join the study, some screening tests will be done first to see if you are eligible. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- You will be asked about your medical history and current medications you are taking.
- You will have a physical examination including vital signs, weight and height.
- You will have routine blood work and blood collected for research purposes.
- You will have a CT scan (multiple x-ray images) or MRI scan (multiple magnetic images).

If the screening information shows that you meet the requirements, then you will be able to start the study. If the screening information shows that you cannot be in the research study, the study doctors will discuss other options with you and/or refer you back to your regular doctor.

During the study:

If the exams, tests and procedures show that you can be in the study, and you choose to take part, then you will be asked to participate in the following tests and procedures.

- You will have a CT or MRI at the point prior to surgery when we review the amount of cancer in your body. **Then you will have combined chemotherapy and radiation therapy for up to 6 weeks**. Combined chemotherapy and radiation therapy is a standard and usual treatment for your cancer, so this is not part of the research study.
- You will have a physical examination including vital signs, weight and a discussion of your current medications once a week for 8 weeks, while you are being treated. For the first 5 days of treatment, you will have a physical exam every other day.
- **You will take doxycycline, the research drug, for 8-10 weeks** (at the same time that you are receiving combined chemotherapy and radiation therapy).
- You will have routine blood work once a week for 8-10 weeks, while you are on treatment.

- Blood will be collected for research purposes on days 1, 3, and 5, 8, 15, 22, 29, at restaging, prior to surgery and again at the time of surgery. With the exception of days 3 and 5, these blood collections with coincide your blood work done for routine clinical purposes. The research blood collected will be used to measure the level of doxycycline in your blood.
- You will have surgery approximately 3-5 weeks after completing the chemoradiation portion of your treatment, and after you have completed the Doxycycline portion of your treatment.

IMPORTANT TO UNDERSTAND:

- Following surgery, the routine procedure at this hospital is to send all removed pancreatic tissue removed to a hospital Pathologist, who does a standard evaluation of the amount of cancer in the tissue, evaluation of how the tumor responded to treatment you have already received (radiation and chemotherapy) and saves some of tissue in case (at some later time) there is interest in analyzing it again or obtaining a second opinion.
- If you decide to participate in this study, this routine procedure will not be followed. Instead, Dr. Tsai will either send the approximately 75% of the main part of the tumor to a collaborating research laboratory (the Massachusetts Institute of Technology) to measure the impact of doxycycline therapy or this will be done at the Medical College of Wisconsin. The tumor slides will be stored at the Medical College of Wisconsin. Only 25% of the tumor, as well as the edges of the tumor (margins) and removed lymph nodes will remain at Froedtert Hospital and will be examined by the hospital Pathologist in the usual manner.
- If you decide to participate in this study, there may not be enough tumor to determine the extent of the tumors involvement with adjacent organs (including small bowel and bile duct). For this reason, the pathologist may not be able to provide a complete report regarding the extent of the tumors involvement with adjacent organs (including small bowel and bile duct). If this is the case, then the tumor stage (T stage) will not be reported in the final pathology report. In addition, there may not be enough tumor available to assess response to the treatment you have already received and may not be available for any future analysis. This may limit your ability to participate in future therapies or clinical trials which require analysis of your primary tumor to determine treatment.
- This may also limit your ability to get a second opinion.

B2. HOW LONG WILL I BE IN THE STUDY?

You will be in this research study for about 5 months. You will be followed up to 60 days from the end of study treatment using review of medical records or telephone contact to assess for adverse events.

B3. CAN I STOP BEING IN THE STUDY?

You are free to withdraw from the study at any time. If you are thinking about leaving, please tell the study doctor.

Dr. Tsai may take you out of this study at any time. This would happen if:

- They think it is in your best interest.
- You do not follow the study rules.
- The whole study is stopped.

If this happens, the study doctor will tell you.

C1. WHAT HEALTH RISKS OR PROBLEMS CAN I EXPECT FROM THE STUDY?

There are risks to taking part in any research study. There is a risk that doxycycline does not help your condition or may make it worse. There also may be problems (side effects) we do not know about yet, from doxycycline itself, or how it combines with chemotherapy or radiation therapy. If we learn about new important side effects, we will tell you.

We watch everyone in the study for problems (side effects). **You need to tell the study doctor or a member of the study team immediately if you experience any problems, side effects, or changes in your health.**

C2. RISKS OF DOXYCYCLINE

Doxycycline may cause problems (side effects). Side effects may be mild or very serious. Some can last a long time or never go away.
The risks with prolonged therapy with doxycycline include:

- abdominal discomfort, cramping, diarrhea
- inflammation of the colon caused by something infectious
- heightened or painful sensitivity to sunlight or ultraviolet light

Combined chemotherapy and radiation therapy is a standard and usual treatment for pancreatic cancer; this is not part of the research study. You will be monitored closely for treatment-related toxicity throughout your participation in the study.

C3. OTHER RISKS OF THIS RESEARCH STUDY

Combined chemotherapy and radiation therapy is a standard and usual treatment for pancreatic cancer; this is not part of the research study. You will be monitored closely for treatment-related toxicity throughout your participation in the study.

There is a risk that the series of extra blood draws (to monitor Doxycycline levels) during the study may be associated with bruising or pain at the site of the blood draw. Repeated blood draws may be associated with a low red blood cell level (anemia) but this is not expected given the amount of blood that we will be collecting.

As already discussed, approximately 75% of the tumor tissue will be used for research and will not be saved at Froedtert, so this tissue will not be available for re-analysis or second opinions in the future. The tumor may not be available at Froedtert for the

hospital pathologist to evaluate the tumor extension into adjacent organs (small bowel or bile duct) or how well your tumor responded to chemotherapy and radiation.

D1. ARE THERE ANY COSTS TO BEING IN THE STUDY?

Most of the medical care that you will receive in this study is considered routine care for your condition and would be recommended whether you join the study or not. Costs for routine care will be billed to you or your insurance carrier. Activities / costs that are part of the study will not be billed to you or your insurance company. These are research blood draws/tests and doxycycline. The cost associated with the research draws and doxycycline will be covered by the trial. Some insurers will not pay for drugs, tests or hospitalization that are part of research studies, so check with your insurer before you join this study. If you have questions regarding study costs, please contact Dr. Tsai.

If you participate in this research study, the costs of any necessary emergency medical treatment in the event of a research-related injury will be billed to you or your health insurance.

D2. WILL I BE PAID FOR PARTICIPATING IN THE STUDY?

There is no payment for being in this study.

D3. WHAT OTHER HEALTHCARE CHOICES DO I HAVE?

You do not have to join this study. You are free to say yes or no. If you do not join this study, your doctor can discuss other healthcare choices with you. Your other choices may include:

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

The study doctor can explain both the possible benefits and the risks of other options that are available to you.

D4. WILL I BE GIVEN NEW INFORMATION ABOUT THE STUDY?

If we learn any important new information about the safety or effectiveness of doxycycline for patients with operable pancreatic cancer that might change your mind about being in the study, we will tell you about it right away. You can then decide if you want to stay in the study.

D5. WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THE STUDY?

Emergency medical treatment for injuries directly related to your participation in this research study will be provided to you. You or your health insurance will be billed for the costs of this emergency treatment. MCW will decide on a case by case basis if they will reimburse you or your insurer for emergency treatment costs. If your research-related injury requires medical care beyond this emergency treatment, you or your insurer will be responsible for the costs of this follow-up care.
At this time, there is no plan for any additional financial payments.

If you believe that you have been injured because of your participation in this study, contact the study doctors right away. Contact information: Susan Tsai, 414-805-9720.

Nothing in this consent form affects any legal rights you may have nor does it release the investigator, the sponsor, the institution, or its agents from liability for negligence.

D6. WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?

- If you have more questions about this study at any time, you can call Dr. Tsai at 414-805-9720.
- If you have questions about your rights as a study participant, want to report any problems or complaints, obtain information about the study, or offer input, you can call the MCW/Froedtert Hospital Research Subject Advocate at 414-955-8844.

E. PERMISSION TO COLLECT, USE AND SHARE HEALTH INFORMATION

E1. What health information will be collected and used for this study?

To be in this research study, the study team needs your permission to access, collect and use some of your health information. If you say no, you cannot be in the study. This information may come from questions we ask, forms we ask you to fill out, or your medical record, as described below. We will only collect and use information needed for the study.

The protected health information (PHI) originates from services you will or have received at one or more of the following locations: the Medical College of Wisconsin (MCW); Children's Hospital of Wisconsin (CHW); any Froedtert Health Affiliate-Froedtert Memorial Lutheran Hospital (FMLH), Inc.; Community Memorial Hospital (CMH) Menomonee Falls, Inc.; St. Joseph's Community Hospital (SJH) West Bend, Inc.; Froedtert & The Medical College of Wisconsin Community Physicians Clinics, Inc. (FMCWCP); the West Bend Surgery Center, LLC; and the Froedtert Surgery Center, LLC.

The health information to be collected and used for this study is:

Past medical records and records dating from when you join this study until the end of the study.

E2. Who will see the health information collected for this study?

The only MCW/Froedtert Hospital employees allowed to handle your health information are those on the study team, those on the Institutional Review Board (IRB) and those who check on the research activities to make sure the hospital's rules are followed.

If the costs of any necessary emergency medical treatment in the event of a research-related injury are billed to your health insurance, your health information may need to be disclosed to the insurer for billing purposes.

The study team may share your information with people who don't work at MCW/Froedtert Hospital because they planned, pay for, or work with us on this study. The federal Privacy Rule may no longer protect your health information once it leaves MCW/Froedtert Hospital. For this study, we plan to share information with those doctors, researchers or government representatives working with us on this study at the institutions or companies listed here:

- Medical College of Wisconsin/Froedtert Internal Review Board
- Wisconsin State Hygiene Laboratory
- Massachusetts Institute of Technology
- Hepatochem

Because this study involves the use of drugs and/or devices, the FDA also has the right to inspect all study records.

We may record your research information, including results of tests and procedures done for research, in your Froedtert Hospital and/or Medical College of Wisconsin medical record. As a result, this research information may be seen by people allowed to see your medical records for healthcare operations or treatment, by those you allow to see your medical records by giving written permission, and by others when required by law.

We will not use your personal health information for a different study without your permission or the permission of a hospital research review board (IRB). Once all personal identification is removed, the information might be used or released for other purposes without asking you. Results of the study may be presented in public talks or written articles, but no information will be presented that identifies you.

E3. What are the risks of sharing this health information?
One risk of taking part in a research study is that more people will handle your personal health information collected for this study. The study team will make every effort to protect the information and keep it confidential, but it is possible that an unauthorized person might see it. Depending on the kind of information being collected, it might be used in a way that could embarrass you or affect your ability to get insurance. If you have questions, you can talk to the study doctor about whether this could apply to you.

E4. How long will you keep the health information for this study?
If you sign this form, we plan to keep your information without any end-date in case we need to check it again for this study.

E5. Can I cancel my permission to share this health information?
If you change your mind later and do not want us to collect or share your health information, you need to send a letter to:

Susan Tsai, MD, MHS
Division of Surgical Oncology
Froedtert Hospital and the Medical College of Wisconsin
9200 W. Wisconsin Ave.
Milwaukee, WI 53226

The letter must say that you have changed your mind and do not want the researcher to collect and share your health information. At that time, we may decide that you cannot continue to be part of the study. We may still use the information we have already collected.

F1. FOR MORE INFORMATION ABOUT THE STUDY
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.

You can look up this study by referring to the ClinicalTrials.gov number 02775695 or by asking the study team for a printed copy.

CONSENT TO PARTICIPATE IN THE STUDY

By signing my name below, I confirm the following:

- I have read (or had read to me) this entire consent document. All of my questions have been answered to my satisfaction.
- The study's purpose, procedures, risks and possible benefits have been explained to me.
- I agree to let the study team use and share the health information and other information gathered for this study.
- I voluntarily agree to participate in this research study. I agree to follow the study procedures as directed. I have been told that I can stop at any time.

IMPORTANT: You will receive a signed and dated copy of this consent form. Please keep it where you can find it easily. It will help you remember what we discussed today.

Subject's Name *please print*	**Subject's Signature**	**Date**
Name of Witness (if applicable) *please print* (for short form consent process, or consent of blind or illiterate subject)	**Signature of Witness**	**Date**

*** Name of person discussing/ obtaining consent** *please print*	**Signature of person discussing/obtaining consent**	**Date**

** A member of the study team trained and authorized by the Principal Investigator to act on her/his behalf in obtaining informed consent according to the protocol. In all research study protocols the Principal Investigator is responsible and accountable for the study.*