Informed Consent Form

A Single-arm Feasibility Study of Gemcitabine, Cisplatin, and Nab-Paclitaxel as Neoadjuvant Therapy for Resectable Oncologically High-Risk Intrahepatic Cholangiocarcinoma

NCT Number: NCT03579771

Document IRB Approval Date: 5/19/2021

EMORY | WINSHIP CANCER INSTITUTE

A Cancer Center Designated by the National Cancer Institute

You Are Being Asked to Be in a Research Study

What Is a Research Study?
The main purpose of research studies is to gain knowledge that may be used to help others. Although it is possible to directly benefit you by participating in a research study, these research studies are not intended to necessarily benefit the patients that participate in them.

Do I Have to Do This?
No. Being in this study is entirely your choice. If you decide to join this study, you can change your mind later on and withdraw from the research study.

Taking part in a study is separate from medical care. The decision to join or not join the research study will not affect your status as a patient.

What Is This Document?
This form is an informed consent document. It will describe the study risks, procedures, and any costs to you.

This form is also a HIPAA Authorization document. It will describe how your health information will be used and by whom.

Signing this form indicates you are willing to take part in the study and allow your health information to be used.

What Should I Do Next?
1. Read this form, or have it read to you.
2. Make sure the study doctor or study staff explains the study to you.
3. Ask questions (e.g., time commitment, unfamiliar words, specific procedures, etc.)
4. If there will be medical treatment, know which parts are research and which are standard care.
5. Take time to consider this, and talk about it with your family and friends.

Emory University and Saint Joseph's Hospital
Consent to be a Research Subject / HIPAA Authorization

Title: A Single-arm Feasibility Study of Gemcitabine, Cisplatin, and Nab-Paclitaxel as Neoadjuvant Therapy for Resectable Oncologically High-Risk Intrahepatic Cholangiocarcinoma

Principal Investigator: Shishir K. Maithel, MD

Study-Supporter: Celgene

Introduction
You are being asked to be in a medical research study. This form is designed to tell you everything you need to think about before you decide if you want to be a part of the study. **It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study.** The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.

Before making your decision:
- Please carefully read this form or have it read to you
- Please listen to the study doctor or study staff explain the study to you
- Please ask questions about anything that is not clear

You can take a copy of this consent form, to keep. Feel free to take your time thinking about whether you would like to participate. You may wish to discuss your decision with family or friends. Do not sign this consent form unless you have had a chance to ask questions and get answers that make sense to you. By signing this form you will not give up any legal rights.

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.

What is the purpose of this study?
The purpose of this study is to examine the ability to give a novel chemotherapy regimen prior to attempted resection of an intrahepatic cholangiocarcinoma that has characteristics that make it very high risk for not being able to be removed or for coming back after it has been removed. The purpose is also to study the effect of the chemotherapy on the tumor and its ability to come back after being removed. The chemotherapy drugs used in this regimen are all FDA approved for treating patients. The application of this regimen for this specific indication in the preoperative setting is investigational. We expect to enroll about 34 patients in this study. Emory will enroll about 12 patients.

What will I be asked to do?
You are being invited to participate in this study because you have recently been diagnosed with intrahepatic cholangiocarcinoma, or bile duct cancer inside the liver. The standard recommendation is to undergo surgery where part of your liver is removed and the lymph nodes around your liver are removed as well. There are

features of your tumor which make it high-risk for coming back after surgery. In this study, we are studying the ability of a patient to receive and tolerate 3 months of chemotherapy prior to undergoing surgery. You will receive 3 months of chemotherapy prior to undergoing surgery. The chemotherapy will consist of 3 different drugs, namely gemcitabine, cisplatin, and nab-Paclitaxel. The gemcitabine / cisplatin / nab-Paclitaxel are given as part of a 3-week cycle, where you receive chemotherapy on day 1 and day 8 of the 21-day cycle. This will continue for 4 cycles, which equals a total of 12 weeks. After the chemotherapy is done and you have recovered, you will be re-evaluated for surgery with imaging scans. If the cancer is stable or improved, you will undergo surgery to remove your tumor. If the cancer has spread to other parts of your body, then you may not undergo surgery. After all the treatment is done, you will continue to undergo imaging studies (CT and/or MRI) every 4 months for 3 years after surgery or until the cancer has returned, whichever comes first. If you are a woman of child-bearing potential, you will be asked to have a pregnancy test. You will also undergo a physical examination and undergo baseline laboratory tests to ensure that you are eligible for this study.

CT Scan: A CT scan allows your doctor to see inside your body to look at the size of your tumor(s). For the CT scan, you may be given a contrast liquid to drink. Or, an IV (intravenous) line may be started by a needle stick in the arm so a contrast liquid can be injected through the line. The IV contrast liquid is a special dye used to get clearer pictures of your body. You will lie flat on a table that will move you into the CT scanner, which is a large, tunnel-shaped machine. You will be asked to lie still and may be asked to hold your breath for a few seconds. The CT scan takes about 30 to 60 minutes and is considered a part of your standard medical care.

MRI Scan: An MRI scan also allows your doctor to see inside your body to see the size of your tumor(s). You may be given gadolinium (a contrast liquid) through a vein in your arm. Gadolinium is a liquid that causes some tumors to appear much brighter than normal tissue on MRI scans. Before gadolinium is injected, the tumor may not be visible. An intravenous (IV) catheter (a tiny tube) may be placed in your arm to inject the contrast liquid. You will then lie on a table that will move into a large tunnel-shaped machine (similar to a CT scan). The MRI scan uses radio frequency waves (like those in an AM/FM radio) and a strong magnet to create a picture of your tumor(s). The MRI scan takes about 60 minutes and is considered a part of your standard medical care.

Who owns my study information and samples?
If you join this study, you will be donating your samples and study information. You will not receive any compensation if your samples or information are used to make a new product. If you withdraw from the study, data and samples that were already collected may be still be used for this study.

What are the possible risks and discomforts?
There may be side effects from the study drugs that are not known at this time.

Gemcitabine

The most common risks and discomforts (>20% of patients):

- Flu-like symptoms of muscle pain, fever, headache, chills and fatigue
- Nausea, vomiting
- Rash
- Hair loss
- Infection, especially when white blood cell count is low
- Bruising, bleeding
- Anemia which may require a blood transfusion

- Muscle weakness
- Blood in urine
- Feeling of "pins and needles" in arms and legs
- Numbness and tingling of the arms and legs
- Tiredness
- Difficulty sleeping
- Hearing loss
- Swelling of arms, legs

The less common risks and discomforts (4-20%):

- Diarrhea, constipation
- Sores in mouth which may cause difficulty swallowing
- Shortness of breath
- Fluid in the organs which may cause low blood pressure, shortness of breath, swelling of ankles
- Brain damage, Reversible Posterior Leukoencephalopathy Syndrome, which may cause headache, seizure, blindness

Rare but possible risks (<4%):

- Abnormal heartbeat
- Heart failure or heart attack which may cause shortness of breath, swelling of ankles, and tiredness
- Blisters on the skin
- Sores on the skin
- Blood clot
- Liver damage which may cause yellowing of eyes and skin, swelling
- Damage to organs which may cause shortness of breath
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Kidney damage which may require dialysis
- Scarring of the lungs
- Fluid around lungs
- Blockage of the airway which may cause cough

Cisplatin

The most common risks and discomforts (>20% of patients):

- Nausea, vomiting
- Infection, especially when white blood cell count is low
- Anemia, which may cause tiredness, or may require blood transfusions
- Bruising, bleeding
- Kidney damage, which may cause swelling
- Hearing decrease,
- Ringing in ears
- Change in taste

The less common risks and discomforts (4-20%):

- Allergic reaction, which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Confusion
- Difficulty with balance
- Numbness in the fingers and toes
- Low blood pressure
- Low magnesium, which may cause heart beat irregularities that are possible life threatening

Rare but possible risks (<4%):
- Cancer of bone marrow later in life caused by chemotherapy
- Seizure

nab-Paclitaxel

The most common risks and discomforts (>20% of patients):
- Anemia, which may cause tiredness, or may require blood transfusions
- Infection, especially when white blood cell count is low
- Diarrhea, nausea
- Pain
- Numbness and tingling of the arms and legs
- Tiredness
- Hair loss

The less common risks and discomforts (4-20%):
- Abnormal heartbeat
- Heart stops beating
- Cloudiness of the eye, visual disturbances
- Vomiting
- Swelling of the body
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Mini stroke
- Paralysis, weakness, headache
- Stroke
- Blood clot which may cause swelling, pain, shortness of breath
- Hoarseness

Rare but possible risks (<4%):
- Bruising, bleeding
- Lung collapse which may cause chest pain

If you are a woman: Women of child-bearing potential (defined as a sexually mature woman who (1) has not undergone hysterectomy [the surgical removal of the uterus] or bilateral oophorectomy [the surgical removal of both ovaries] or (2) has not been naturally postmenopausal for at least 24 consecutive months [i.e., has had

menses at any time during the preceding 24 consecutive months]) must commit to true abstinence from heterosexual contact (which must be reviewed on a monthly basis), or agree to use, and be able to comply with, effective contraception without interruption for 28 days prior to starting gemcitabine/cisplatin/nab-paclitaxel (including dose interruptions) until treatment with gemcitabine/cisplatin/nab-paclitaxel is complete.

If you are a man: Male subjects must practice true abstinence or agree to use a condom during sexual contact with a female of childbearing potential or a pregnant female while on treatment (including during dose interruptions) with gemcitabine/cisplatin/nab-paclitaxel and for 6 months following gemcitabine/cisplatin/nab-paclitaxel discontinuation, even if he has undergone a successful vasectomy.

Contrast Agent
Your CT or MRI procedure will require the use of a "contrast agent." The contrast agent is a substance that helps the radiologist interpret the images. The contrast agent will be injected by either a hand-held needle or a machine that does the injection. Most contrast agents stay in your body for only a few minutes, but some of them can remain for a few hours or days without any harm to you or anyone near you. Contrast agents are generally quite safe, but any injection involves some risks. The injection could harm a nerve, artery or vein, or cause infection. The contrast agent could affect kidney function or cause an allergic reaction, though these outcomes are rare. The contrast agent could also leak from your veins a little causing swelling and discomfort, that is typically treated with ice packs.

MRI
MRI exams use powerful magnets to create images of the body. In addition to the possible reactions to contrast materials, you may feel claustrophobic while in the magnet, and will hear loud beeping or hammering noises. If you have tattoos or any metal items in your body such as implants, pacemakers, clips or shrapnel, we will do special screening to make sure your MRI scan is done safely.

Radiation-Related Risks
You will be exposed to radiation from CT scans. These procedures are necessary for your medical care and will occur even if you do not participate in this study. The radiation dose estimate that you will receive is equal to or less than the radiation exposure allowed to be received by a radiation worker for 4 years. The principal risk associated with a radiation dose is the possibility of developing a radiation-induced cancer later in life. Although the risk from radiation is cumulative it is not expected to adversely affect your condition or treatment. The Emory University Radiation Safety Committee has reviewed and approved the use of radiation in this research study.

Will I benefit directly from the study?
This study is not designed to benefit you directly. Your disease may improve while you are in this study but it may not, and it may even get worse. This study is designed to learn more about whether receiving this chemotherapy regimen before undergoing surgery for intrahepatic cholangiocarcinoma is feasible. The study results may be used to help others in the future.

Will I be compensated for my time and effort?
You will not be offered compensation for being in this study.

What are my other options?

If you decide not to enter this study, there is care available to you outside of this research study. The study doctor will discuss these with you. You do not have to be in this study to be treated for intrahepatic cholangiocarcinoma.

Taking part in this study, however, may make you unable to participate in some other research studies, if they exclude people who have taken certain treatments. You should discuss this with the researchers if you have concerns. You may wish to research other study options at websites like clinicaltrials.gov and ResearchMatch.org.

How will you protect my private information that you collect in this study?
Whenever possible, a study number, rather than your name, will be used on study records. Your name and other identifying information will not appear when we present or publish the study results.

Study records can be opened by court order. They also may be provided in response to a subpoena or a request for the production of documents.

Storing and Sharing your Information
De-identified data from this study, including your de-identified genetic information, may be shared with the research community at large to advance science and health. Data from this study may be placed into public databases where, in addition to having no direct identifiers, researchers will need to sign data use agreements before accessing the data. We will remove or code any personal information that could identify you before your information is shared. This will ensure that, by current scientific standards and known methods, it is extremely unlikely that anyone would be able to identify you from the information we share. Despite these measures, we cannot guarantee anonymity of your personal data.

Medical Record
If you have been an Emory and Saint Joseph's Hospital patient before, then you already have an Emory and Saint Joseph's Hospital medical record. If you have never been an Emory and Saint Joseph's Hospital patient, you do not have one. An Emory and Saint Joseph's Hospital medical record will be made for you if an Emory and Saint Joseph's Hospital provider or facility gives you any services or procedures for this study.

Copies of the consent form/HIPAA authorization that you sign will be put in any Emory and Saint Joseph's Hospital medical record you have now or any time during the study.

Emory and Saint Joseph's Hospital may create study information about you that can help with your care. For example, the results of study tests or procedures. These study results will be put in your Emory and Saint Joseph's Hospital medical record. Anyone who has access to your medical records will be able to have access to all the study information placed there. The confidentiality of the study information in your medical record will be protected by laws like the HIPAA privacy rule. State and federal laws may not protect the research information from disclosure.

Tests and procedures done at non-Emory and Saint Joseph's Hospital places may not become part of your Emory and Saint Joseph's Hospital medical record. Also, if you decide to be in this study, it is up to you to let your other health providers know.

In Case of Injury

If you get ill or injured from being in the study, Emory and Saint Joseph's Hospital will help you get medical treatment. Emory and Saint Joseph's Hospital and the study supporter have not, however, set aside any money to pay you or to pay for this medical treatment. The only exception is if it is proven that your injury or illness is directly caused by the negligence of an Emory and Saint Joseph's Hospital or study supporter employee. "Negligence" is the failure to follow a standard duty of care.

If you become ill or injured from being in this study, your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurer does not pay, then you will have to pay these costs.

If you believe you have become ill or injured from this research, you should contact Dr. Maithel at telephone number [redacted]. You should also let any health care provider who treats you know that you are in a research study.

Costs

The study supporter will pay for certain items and services that you may receive if you take part in this study.

You will have to pay for the items or services for which the study supporter does not pay. The study supporter will not pay for your regular medical care. If you have insurance, Emory and Saint Joseph's Hospital will submit claims to your insurance for items and services that the study supporter does not cover. Emory and Saint Joseph's Hospital will send in only those claims for items and services that it reasonably believes your insurance will pay and that the study supporter has not paid.

The actual amount that you have to pay depends on whether or not you have health insurance and whether or not that insurance will pay for any research study costs. Generally, insurance companies will not pay for items and services that are required just for a research study. Some insurance companies will not pay for regular medical treatment or treatment for complications if you are in a study. How much you will have to pay for any co-payments, deductibles or co-insurance depends on your plan. Emory and Saint Joseph's Hospital and the study supporter will not pay for these costs.

It is a good idea to contact your insurance provider and tell them you want to be in this research study. Ask them what they will pay for and what they will not pay for. You can also ask the study team for help in figuring out what you will have to pay.

If you do not have insurance, Emory and Saint Joseph's Hospital will review your case as part of its program for low-income patient care. The standard policies of that program will apply. The program will figure out if you have to pay any costs for taking part in the study and what those costs will be.

Withdrawal from the Study

You have the right to leave a study at any time without penalty.

For your safety, however, you should consider the study doctor's advice about how to go off the study treatment. If you leave the study before the final planned study visit, the researchers may ask you to have some of the final steps done.

The researchers also have the right to stop your participation in this study without your consent for any reason, especially if they believe it is in your best interest or if you were to object to any future changes that may be made in the study plan.

Authorization to Use and Disclose Protected Health Information

The privacy of your health information is important to us. We call your health information that identifies you, your "protected health information" or "PHI." To protect your PHI, we will follow federal and state privacy laws, including the Health Insurance Portability and Accountability Act and regulations (HIPAA). We refer to all of these laws as the "Privacy Rules." Here we let you know how we will use and disclose your PHI for the study in which you may choose to participate.

PHI that Will be Used/Disclosed:
The PHI that we will use or share for the research study includes:

- Medical information about you including your medical history and present/past medications.
- Results of exams, procedures and tests you have before and during the study.
- Laboratory test results.

Purposes for Which Your PHI Will be Used/Disclosed:
We will use and share your PHI for the conduct and oversight of the research study. We will use and share your PHI to provide you with study related treatment and for payment for such treatment. We will also use and share your PHI to conduct normal business operations. We may share your PHI with other people and places that help us conduct or carry out the study, such as laboratories, data management centers, data monitors, contract research organizations, Institutional Review Boards (IRBs) and other study sites. If you leave the study, we may use your PHI to determine your health, vital status or contact information. We will use and disclose your PHI for the administration and payment of any costs relating to subject injury from the study.

Use and Disclosure of Your Information That is Required by Law:
We will use and disclose your PHI when we are required to do so by law. This includes laws that require us to report child abuse or abuse of elderly or disabled adults. We will also comply with legal requests or orders that require us to disclose your PHI. These include subpoenas or court orders.

Authorization to Use PHI is Required to Participate:
By signing this form, you give us permission to use and share your PHI as described in this document. You do not have to sign this form to authorize the use and disclosure of your PHI. If you do not sign this form, then you may not participate in the research study or receive research-related treatment. You may still receive non-research related treatment.

People Who will Use/Disclose Your PHI:
The following people and groups will use and disclose your PHI in connection with the research study:

- The Principal Investigator and the research staff will use and disclose your PHI to conduct the study and give you study related treatment.
- Emory may use and disclose your PHI to get payment for study related treatment and to run normal business operations.
- The Principal Investigator and research staff will share your PHI with other people and groups to help conduct the study or to provide oversight for the study.

- Winship Cancer Institute is the lead institution of the study. They may use and disclose your PHI to make sure the research is done correctly and to collect and analyze the results of the research. They may disclose your PHI to other people and groups like study monitors to help conduct the study or to provide oversight for the study.
- The research team and the Study supporter may use and disclose your PHI, including disclosure to insurance carriers to administer payment for subject injury.
- The following people and groups will use your PHI to make sure the research is done correctly and safely:
    - Emory offices that are part of the Human Research Participant Protection Program and those that are involved in study administration and billing. These include the Emory IRB, the Emory Research and Healthcare Compliance Offices, and the Emory Office for Clinical Research.
    - Government agencies that regulate the research including: Food and Drug Administration.
    - Public health agencies.
    - Research monitors and reviewer.
    - Accreditation agencies.
    - Study supporter: Celgene
- Sometimes a Principal Investigator or other researcher moves to a different institution. If this happens, your PHI may be shared with that new institution and their oversight offices. PHI will be shared securely and under a legal agreement to ensure it continues to be used under the terms of this consent and HIPAA authorization.

Expiration of Your Authorization
Your PHI will be used until this research study ends.

Revoking Your Authorization
If you sign this form, at any time later you may revoke (take back) your permission to use your information. If you want to do this, you must contact the study team at:

Shishir K. Maithel, MD
Winship Cancer Institute, Emory University
1365-C Clifton Road NE
Atlanta, GA 30322

At that point, the researchers would not collect any more of your PHI. But they may use or disclose the information you already gave them so they can follow the law, protect your safety, or make sure that the study was done properly and the data is correct. If you revoke your authorization you will not be able to stay in the study.

Other Items You Should Know about Your Privacy
Not all people and entities are covered by the Privacy Rules. HIPAA only applies to health care providers, health care payers, and health care clearinghouses. If we disclose your information to people who are not covered by the Privacy Rules, including HIPAA, then your information won't be protected by the Privacy Rules. People who do not have to follow the Privacy rules can use or disclose your information with others without

your permission if they are allowed to do so by the laws that cover them. The Study supporter, and people and companies working with the Study supporter on this study are not covered by the Privacy Rules. They will only use and disclose your information as described in this Consent and Authorization.

To maintain the integrity of this research study, you generally will not have access to your PHI related to this research until the study is complete. When the study ends, and at your request, you generally will have access to your PHI that we maintain in a designated record set. A designated record set is data that includes medical information or billing records that your health care providers use to make decisions about you. If it is necessary for your health care, your health information will be provided to your doctor.

We may remove identifying information from your PHI. Once we do this, the remaining information will not be subject to the Privacy Rules. Information without identifiers may be used or disclosed with other people or organizations for purposes besides this study.

Contact Information

Contact Dr. Shishir Maithel at [redacted]:

- if you have any questions about this study or your part in it,
- if you feel you have had a research-related injury or a bad reaction to the study drug, or
- if you have questions, concerns or complaints about the research

Contact the Emory Institutional Review Board at [redacted]:

- if you have questions about your rights as a research participant.
- if you have questions, concerns or complaints about the research.
- You may also let the IRB know about your experience as a research participant through our Research Participant Survey at http://www.surveymonkey.com/s/6ZDMW75.

Consent and Authorization

TO BE FILLED OUT BY SUBJECT ONLY

Please **print** your name, **sign**, and **date** below if you agree to be in the main study. By signing this consent and authorization form, you will not give up any of your legal rights. We will give you a copy of the signed form to keep.

_____
Name of Subject

_____ _____ ____:____ **am / pm**
Signature of Subject (18 or older and able to consent) **Date** **Time (please circle)**

TO BE FILLED OUT BY STUDY TEAM ONLY

_____
Name of Person Conducting Informed Consent Discussion

_____ _____ ____:____ **am / pm**
Signature of Person Conducting Informed Consent Discussion **Date** **Time (please circle)**