IRB Approved: 11/29/2022
Approval Expires: 11/28/2023

OREGON HEALTH & SCIENCE UNIVERSITY

MED. REC. NO. _____
NAME _____
BIRTHDATE _____

IRB#: 23631

CLINICAL RESEARCH CONSENT AND AUTHORIZATION SUMMARY OF KEY INFORMATION ABOUT THIS STUDY

TITLE: Pancreatic Endotherapy for Refractory Chronic PancreaTitis (PERCePT)

PRINCIPAL INVESTIGATOR: Gregory Cote, M.D., M.S. *(503) 494-5255*

You are being asked to join a research study. This consent form contains important information to help you decide if you want to join the study or not.

PURPOSE:
The purpose of this study is to evaluate whether endoscopic ultrasound (EUS) only versus EUS + endoscopic retrograde cholangiopancreatography (ERCP) with pancreatic endotherapy reduces pain in the treatment of chronic pancreatitis with pancreatic duct obstruction. Chronic pancreatitis is an inflammation and scarring of the pancreas that does not heal or improve—it may get worse over time and lead to further damage of the pancreas. With pancreatic duct obstruction, the pancreatic duct connects the pancreas to the beginning of the small intestine (duodenum). Compression, blockage, or inflammation of the pancreatic duct may lead to abdominal pain.

ERCP with treatment of duct obstruction is one of the standard therapies for chronic pancreatitis with pancreatic duct obstruction. However, this study is being done because the effectiveness of ERCP with treatment of pancreatic duct obstruction is not known.

DURATION:
Your participation in the study will consist of approximately 8 visits over 12 months. Visits will last up to three hours. We may ask to follow your health using medical record review or follow up phone calls for up to 1 year.

PROCEDURES:
If you agree to participate, you will undergo a baseline visit where you will answer questionnaires and interview questions about your pain, quality of life, psychological factors, sleep, opioid use, alcohol use, and pain-related disability. You will also have a test called Quantitative Sensory Testing (QST) to measure how you perceive mild skin pressure and hot sensations. Your medical records will be reviewed to collect information and confirm that EUS is indicated for you. You will also be asked to complete an electronic diary for 14 days on your

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mobile phone or by e-mail or telephone call. Once confirmed that you are able to continue, you will be randomly assigned to either EUS alone or EUS + ERCP with pancreatic endotherapy. You will have a 50:50 chance of being assigned to EUS only (like the flip of a coin). Neither you nor your study doctor will make the choice to which group you are assigned. If you are assigned to the EUS + ERCP with pancreatic endotherapy group, a procedure called extracorporeal shock wave lithotripsy (ESWL) may be done to break up the pancreatic stones.

You will be asked to complete telephone visits at 7 days and 30 days after your procedure. You will also be asked to complete the electronic diary daily for 30 days after your procedure and then again from 76 through 90 days after the procedure. At 90 days, 180 days, 270 days, and 360 days following the procedure, you will be asked to undergo visits in-person or by telephone to complete some of the questionnaires originally completed during the baseline visit. At 90 days, you will be asked to undergo Quantitative Sensory Testing again.

RISKS:
There are some risks to study participation. If you are randomized to EUS + ERCP with pancreatic endotherapy, you will be exposed to the risks of these procedures such as bleeding, pancreatitis, perforation, and infection. If you are randomized to receive only the EUS procedure, then you will not be exposed to the risks of ERCP with endotherapy, but you will also not have the potential benefits of the ERCP with endotherapy.

BENEFITS:
The potential benefit to you is that the treatment you receive may prove to be more effective or less harmful than the other study treatment, although this cannot be guaranteed.

ALTERNATIVES:
You do not have to participate in this study to have your condition treated. The standard therapies for your condition are EUS or ERCP with pancreatic endotherapy (these are the two treatment groups being evaluated in this study).

This is a voluntary research study. You do not have to join the study. Even if you decide to join now, you can change your mind later. Please ask the Investigator if you have any questions about the study or about this consent form.

END OF CONSENT SUMMARY

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Clinical Research Consent and Authorization Form

TITLE: Pancreatic Endotherapy for Refractory Chronic PancreaTitis (PERCePT)

PRINCIPAL INVESTIGATOR: Gregory Cote, M.D., M.S. (503) 494-5255

WHO IS PAYING FOR THE STUDY?: Department of Defense

WHO IS PROVIDING SUPPORT FOR THE STUDY?: OHSU is being compensated by the funder to conduct this study. This is to pay for tests performed only for study purposes, and for the time involved on the part of the investigator(s) and study staff. You may freely discuss this with your physician and the investigator if you have concerns.

Your study doctor and the research staff have no financial involvement with the funder and are not being paid directly by the funder for conducting this study. However, they may have travel expenses covered by the funder to attend study training meetings.

WHY IS THIS STUDY BEING DONE?:
Please read this consent form carefully and take your time making your decision. As your study doctor or study staff discusses this consent form with you, please ask them to explain any words or information that you do not clearly understand.

You are being asked to participate in this study because you have chronic pancreatitis with pancreatic duct obstruction. Chronic pancreatitis is an inflammation and scarring of the pancreas that does not heal or improve—it may get worse over time and lead to further damage of the pancreas. With pancreatic duct obstruction, the pancreatic duct connects the pancreas to the beginning of the small intestine (duodenum). Compression, blockage, or inflammation of the pancreatic duct may lead to abdominal pain.

Endoscopic retrograde cholangiopancreatography (ERCP) with treatment of duct obstruction is one of the standard therapies for your condition. However, this study is being done because the effectiveness of ERCP with treatment of duct obstruction is not known. This study will evaluate whether endoscopic ultrasound (EUS) only versus EUS + endoscopic retrograde cholangiopancreatography (ERCP) with pancreatic endotherapy reduces pain in the treatment of chronic pancreatitis with pancreatic duct obstruction.

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WHAT EXAMS, TESTS AND PROCEDURES ARE INVOLVED IN THIS STUDY?
If you agree to be in this study, the following will happen:

Baseline Visit (approximately 2-3 hours):
You will answer questionnaires about your pain, quality of life, psychological factors, sleep, opioid use, alcohol use, and pain-related disability. These questionnaires will take approximately 60 minutes to complete.

You will also have a test called Quantitative Sensory Testing (QST) to measure how you perceive mild skin pressure and hot sensations. This is being done to quantify and characterize the pain that you feel. For pressure assessments, a plastic-tipped pointed sensor will be placed on your skin and pressure will be applied until you first notice pain. This will be done 12 times.

For hot assessments, a plastic thermode will be attached to your forearm with Velcro. This thermode will be heated by a computer and you will report sensory and pain sensations associated with different temperatures. This procedure will also be done 11 times. These procedures are non-invasive—no needles are used. The tests are time-limited, and the amount of pressure or heating used will not be able to damage your skin or any other tissue. This testing takes approximately 1 hour to complete.

The researchers will check your medical records to gather information about your chronic pancreatitis and confirm that EUS is indicated for you.

You will also be asked to complete an electronic diary on a mobile device or by e-mail or by phone for 14 days before randomization procedures listed below. If you have a smart phone, it will be registered into a diary system that will ask you daily questions about your pain, mood, sleep, and medications. If you do not have a smart phone, we may provide you with a smart phone for use during the study. This can also be completed by e-mail or telephone call. If you decide to discontinue treatment or upon completion of the EMA portion utilizing the phone (90-day mark), you are required to return the phone to study staff. If you are feeling much better at the completion of the 14-day period before randomization, your treating physician may not recommend an intervention (randomization); in this case, you may still be included in the study and participate in scheduled follow-up visits as an observational participant for follow-up visits only . If you agree to continue in the observation group, you may complete follow up visits by telephone.

Randomization (approximately 2 hours):
Approximately two weeks after you complete the baseline visit, you will be randomly assigned to one of the two following groups, like drawing numbers from a hat:

- EUS only
- EUS + ERCP with pancreatic endotherapy.

This means that you will have a 50:50 chance of being assigned to either group. Neither the researchers nor you will make the choice to which group you are assigned, and you will remain blinded to which procedure you were assigned until after your final follow up visit 12 months later. You will undergo anesthesia administered sedation and endoscopic ultrasound (EUS). The endoscopist will confirm that you qualify for the study. Following the completion of the EUS, assuming that eligibility criteria are still met, and while you remain under anesthesia, you will be randomized to ERCP with pancreatic endotherapy or EUS only. If randomized to EUS only, the endoscopist will not perform ERCP.

1. **Pregnancy test:** If you are of childbearing potential you will undergo a pregnancy test. If positive, you will not be enrolled in this study. If negative, you may continue to be enrolled in this study.

2. Endoscopic Ultrasound (EUS): This procedure is frequently performed to diagnose why patients are having chronic episodes of pancreatitis. A bendable, lighted tube (endoscope) about the thickness of your index finger is placed through your mouth and into your stomach and first part of the small intestine (duodenum). The tip of the endoscope has an ultrasound probe, which uses sound waves to produce images of your pancreas and other organs nearby. This procedure is usually done before the ERCP with endotherapy and would occur whether or

not you get randomized to get ERCP with endotherapy. If randomized to EUS only, you will stay in the procedure room for at least 45 minutes.

3. Endoscopic Retrograde CholangioPancreatography (ERCP) with endotherapy is a medical procedure that is often performed in patients with chronic pancreatitis who also have pancreatic duct obstruction. For this procedure, doctors use a combination of x-rays and an endoscope (a long flexible lighted tube) to find the opening of the pancreatic duct where fluid drains out of your pancreas. The doctor then uses endotherapy to treat the compression or inflammation of the pancreatic duct either by dilating the duct with a balloon to help the duct remain open or placing an FDA approved stent (like a straw) in the duct, or both. Endotherapy may also involve lithotripsy or shock waves that can break up any objects that may be blocking the pancreatic duct. The goal of this procedure is to reduce the risk of future attacks of chronic pancreatitis. At the discretion of the treating physician, you may be given a medication called an indomethacin suppository to help prevent post-ERCP pancreatitis. Suppository means the medication will be given rectally. Indomethacin is commonly used to prevent post-ERCP pancreatitis in clinical practice based on previous studies but is not FDA approved for this specific purpose.

4. Extracorporeal shock wave lithotripsy (ESWL) is an adjunct procedure to ERCP which involves the use of a special machine that delivers high frequency shock waves under X-ray guidance into obstructing pancreatic stones. There are no known added risks to ESWL on top of those related to ERCP with endotherapy. After the procedure, your care will be managed primarily by a physician who is blinded to whether you received EUS or EUS +ERCP with endotherapy.

Follow up:
You will also be asked to complete an electronic diary daily for 30 day, starting on the day that you have the EUS alone or EUS + ERCP with pancreatic endotherapy procedure. You will be asked to complete an electric diary again 76-90 days after the EUS alone or EUS + ERCP with pancreatic endotherapy procedure.

You will be asked to complete visits over the phone at 7 days and again at 30 days after your procedure. The telephone visits will take approximately 15 minutes and will involve asking you about any adverse events you may have experienced after the procedures and to make sure that you are completing your electronic diary daily.

At 90 days, you will be asked to undergo Quantitative Sensory Testing again if you are in the randomized study. This visit will take approximately 2 hours to complete.

At 180 days, 270 days, and 360 days following the procedure, you will be asked to undergo visits in-person or by telephone to complete some of the questionnaires originally given to you at the baseline visit. The 90-day in-person visit will take approximately 2 hours to complete, while the other follow-up visits are expected to take approximately 1 hour to complete.

WHAT RISKS CAN I EXPECT FROM TAKING PART IN THIS STUDY?:

The following risks apply only to those randomized to receive ERCP with endotherapy:

ERCP with endotherapy
The ERCP with pancreatic endotherapy has risks, which your doctor will discuss with you. These risks include:

Pancreatitis: This is the most common side effect of ERCP. It occurs after about 5-10% of ERCP procedures and generally involves hospital admission. Very rare severe cases may result in formation of a pancreatic pseuodcyst or abscess, and/or the heart, lungs, or kidneys may fail.

Endotherapy: The risks of endotherapy involve bleeding around the site, infection, or obstruction caused by the fragments of material created by the endotherapy that may require more endotherapy to remove.

Indomethacin: Long or medium-term use of non-steroidal anti-inflammatory drugs (NSAIDs), such as indomethacin, is associated with several adverse events including peptic ulcer disease, kidney failure, heart attack, stroke, and worsening of congestive heart failure or high blood pressure. The risk of these adverse events, however, is related to the duration of use. A single dose of indomethacin is extremely unlikely to cause the biochemical, hormonal, and physiologic changes necessary to induce such events.

Stent Placement: There is a chance that the stent could be placed within or migrate into the duct and cause pancreatitis, infection, or perforation. Migrated stents can be difficult to retrieve and may require an operation. This is an extremely unlikely event.

The following risks apply only to those randomized to the EUS only procedure:

Not receiving ERCP
If you are in the EUS only group, you will not receive ERCP with endotherapy. You will not be exposed to the risks specific to ERCP, including acute pancreatitis related to the ERCP itself. However, you will not receive any potential benefit that could occur from the ERCP procedure. Your doctor will discuss the risks of this clinical procedure with you.

The following risks apply to all individuals participating in the study:

Cardiopulmonary
The effects of sedation/anesthesia and the stresses of the EUS & ERCP procedure may result (during procedures or in the early recovery period) in heart or lung issues. Most of these events can be managed by standard conservative means, but some may result in the procedure being aborted, and/or the need for hospitalization.

EUS
Risks of EUS include bleeding, heart or lung problems, infection, or inflammation at the intravenous (IV) site, perforation, and adverse reaction to medication. Your doctor will discuss the risks of this clinical procedure with you.

Extracorporeal Shock Wave Lithotripsy (ESWL)
Risks of ESWL include pancreatitis, bleeding, infection, perforation, and blockage in the pancreas due to a build-up of stone fragments. These complications can occur in 1 in 20 individuals.

General Anesthesia
The most common side effects of general anesthesia include sore throat, nausea, vomiting, and dizziness. When placing a breathing tube, there is a small risk that the anesthesia provider can damage your teeth. With any medication given, you can have an allergic reaction. Even if you have a severe reaction, your anesthesia providers are usually able to treat these reactions early enough to keep you safe. Rare but severe problems from general anesthesia include heart attack, pneumonia, nerve damage and stroke.

Quantitative Sensory Testing
The procedures proposed in this study are widely used in research and clinical practice and have been shown to be safe. For thermal pain procedures, the stimulator will be set with a limit of 50ºC which is well below the threshold for causing any damage to subject's skin or nerve endings. However, it is not unusual to experience some tenderness, redness, or inflammation in the heated skin area after completion of the thermal pain procedures. These symptoms subside within a few hours with no intervention.

Randomization
You will be randomly assigned to receive the EUS procedure only or the EUS + ERCP with endotherapy procedure. The group you are assigned to may prove to be less beneficial to you or have more risks than the other group, or other options for managing your condition outside of this study.

Not knowing which procedure you received
To keep the study free from bias, it is important that neither you nor the clinicians involved in treating you after your study procedure know if you received the EUS or EUS + ERCP with endotherapy procedure. Your medical record will not say which procedure you received. If you were to have a medical problem where it was important for your treatment provider to know if you received ERCP or not, this information isn't readily available. If a situation arises where it is medically necessary to find out if you underwent an ERCP, your study doctor may provide this information.

Confidentiality
All studies carry some risk for the potential loss of confidentiality. Every effort will be made to protect your information.

Interviews & Questionnaires
Some of the questions the researchers ask you may be upsetting, or you may feel uncomfortable answering them. If you do not wish to answer a question, you can skip it and go to the next question.

WHAT ARE MY CHOICES IF I DECIDE NOT TO TAKE PART IN THIS STUDY?

You may choose not to be in this study. The potential benefit to you is that the treatment you receive may prove to be more effective than the other study treatment or than other available treatments, although this cannot be guaranteed. If you are randomized to EUS only, and the study shows that ERCP is not effective, you may be spared the risks of ERCP with endotherapy, and thus you may benefit from participating in the study. If you are randomized to EUS +ERCP with endotherapy, and this procedure proves to be beneficial, then you may benefit from participating in the study. Neither of these potential benefits can be guaranteed.

If you choose not to participate in this study, you could receive other treatments for your condition. Standard therapies for your condition include no interventional procedures (which is similar to the EUS only group), pancreatic endotherapy (which is similar to the EUS + ERCP group), and surgical interventions on the pancreas.

WHO WILL SEE MY PERSONAL INFORMATION?

We will take steps to keep your personal information confidential, but we cannot guarantee total privacy. If you are an OHSU patient, you have an OHSU medical record. Results of research tests or procedures will not be included in your OHSU medical record. A separate medical record for this study only will be created and all procedures will be documented as usual in this record. All information within the study medical record can be viewed by individuals authorized to access the record. We will make every effort to keep confidential all research information in the medical record that identify you to the extent allowed by law. The Department of Defense is granted access to research records as part of its human subjects protection oversight activities.

We will create and collect health information about you as described in the WHY IS THIS STUDY BEING DONE? and the WHAT EXAMS, TESTS AND PROCEDURES ARE INVOLVED IN THIS STUDY? sections of this form. Health information is private and is protected under federal law and Oregon law. By agreeing to be in this study, you are giving permission (also called authorization) for us to use and disclose your health information as described in this form.

The investigators, study staff, and others at OHSU may use the information we collect and create about you to conduct and oversee this research study.

We may release this information to others outside of OHSU who are involved in conducting or overseeing research, including:

- The funder of this study, the Department of Defense

Those listed above may also be permitted to review and copy your records, including your medical records. We will not release information about you to others not listed above, unless required or permitted by law. We will not use your name or your identity for publication or publicity purposes unless we have your special permission.

WILL ANY OF MY INFORMATION OR SAMPLES FROM THIS STUDY BE USED FOR ANY COMMERCIAL PROFIT?

Samples and/or information about you or obtained from you in this research may be used for commercial purposes, such as making a discovery that could, in the future, be patented or licensed to a company, which could result in a possible financial benefit to that company, OHSU, and its researchers. There are no plans to pay you if this happens. You will not have any property rights or ownership or financial interest in or arising from products or data that may result from your participation in this study. Further, you will have no responsibility or liability for any use that may be made of your samples or information.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

Some of the services or items in this study are part of the regular treatment for your condition. These would be performed or used even if you were not in this study. The costs for these services or items will be billed to your insurance. You will be responsible for any costs your insurance does not cover. If you have any questions about these costs, or what out-of-pocket expenses you may be responsible for, contact your insurance company. If you are uninsured, you will be responsible for these costs.

You will not be billed for the costs of any services or procedures that are required by the study but are not considered part of your regular treatment.

You will be compensated $75 after completing the baseline assessments. You will be compensated $50 after completing the 30-day follow-up visit (telephone visit). You will be compensated $75 after completing the 90-day follow-up visit. If you complete all visits, you will be compensated a total of $200.

We may request your social security number to process any payments for participation. Payments that you receive from OHSU for participating in a research study are considered taxable income per IRS regulations. Payment types may include, but are not limited to checks, cash, gift certificates/cards, personal property, and other items of value. If the total amount of payment you receive from OHSU reaches or exceeds $600.00 in a calendar year, you will be issued a Form 1099.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?:

If you believe you have been injured or harmed because of participating in this research and require treatment, contact Gregory Cote at 503-494-5255 or contact the OHSU operator at 503-494-8311 and ask to speak with the GI physician on-call.

If you are injured or harmed by the procedures performed in this study you will be treated. OHSU does not offer any financial compensation or payment for the cost of treatment if you are injured or harmed because of participating in this research. Therefore, any medical treatment you need may be billed to you or your insurance. However, you are not prevented from seeking to collect compensation for injury related to negligence on the part of those involved in the research. Oregon law (Oregon Tort Claims Act (ORS 30.260 through 30.300)) may limit the dollar amount that you may recover from OHSU or its caregivers and researchers for a claim relating to care or research at OHSU, and the time you have to bring a claim.
If you have questions on this subject, please call the OHSU Research Integrity Office at (503) 494-7887.

This federally funded study also does not have the ability to provide compensation for research-related injury. If you are injured or become ill from taking part in this study, it is important to tell your study doctor. Emergency treatment may be available but you or your insurance company will be charged for this treatment.

WHERE CAN I GET MORE INFORMATION?

If you have any questions, concerns, or complaints regarding this study now or in the future, contact Gregory Cote at 503-494-5255.

This research has been approved and is overseen by an Institutional Review Board ("IRB"), a committee that protects the rights and welfare of research participants. You may talk to the IRB at (503) 494-7887 or irb@ohsu.edu if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get more information or provide input about this research.

You may also submit a report to the OHSU Integrity Hotline online at https://secure.ethicspoint.com/domain/media/en/gui/18915/index.html or by calling toll-free (877) 733-8313 (anonymous and available 24 hours a day, 7 days a week).

DO I HAVE TO TAKE PART IN THIS STUDY?

Your participation in this study is voluntary. You do not have to join this or any research study. You do not have to allow the use and disclosure of your health information in the study, but if you do not, you cannot be in the study.

Your health care provider may be one of the investigators of this research study and, as an investigator, is interested in both your clinical welfare and in the conduct of this study. Before entering this study or at any time during the research, you may ask for a second opinion about your care from another doctor who is in no way involved in this project. You do not have to be in any research study offered by your physician.

IF I DECIDE TO TAKE PART IN THIS STUDY, CAN I STOP LATER?

As part of this research study, your study doctor and his/her research team will keep records of your participation in this study.

The health information OHSU may use or disclose (release) for this research study includes information in your medical record, results of physical exams, medical history, lab tests or certain health information indicating or relating to your condition.

Your study doctor and his/her research team will use and disclose (release) your health information to conduct this study. The health information listed above may be used by and/or disclosed (released) to the following, as applicable:

- The sponsor of the study including its agents such as data repositories or contract research organizations monitoring the study;
- Other institutions and investigators participating in the study;
- Data Safety Monitoring Boards;
- Accrediting agencies;
- Clinical staff not involved in the study whom may become involved if it is relevant;
- Parents of minor children if less than 16 years old. Parents of children 16 years old or older require authorization from the child; or
- Health insurer or payer in order to secure payment for covered treatment;
- Federal and state agencies and MUSC committees having authority over the study such as:

The Institutional Review Board (IRB) overseeing this study; Committees with quality improvement responsibilities; Office of Human Research Protections; Food and Drug Administration; National Institutes of Health or Other governmental offices, such as a public health agency or as required by law.

Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it and may share your information with others without your permission, if permitted by laws governing them. You do not have to sign this consent form. If you choose not to sign, it will not affect your treatment, payment or enrollment in any health plan or affect your eligibility for benefits. However, you will not be allowed to be a participant in this research study.

You will be given a copy of this consent form. Your authorization will expire at the conclusion of this study. You have the right to withdraw your agreement at any time. You can do this by giving written notice to your study doctor. If you withdraw your agreement, you will not be allowed to continue participation in this research study. However, the information that has already been collected will still be used and released as described above. You have the right to review your health information that is created during your participation in this study. After the study is completed, you may request this information.

SIGNATURES:

Your signature below indicates that you have read this entire form and that you agree to be in this study.

We will give you a copy of this signed form.

Participant Printed Name	Participant Signature	Date
Person Obtaining Consent Printed Name	Person Obtaining Consent Signature	Date