Phase 1/2 Trial of Indomethacin in Chronic Pancreatitis (The PAIR Trial)

NCT04207060

August 26, 2022

MAYO CLINIC

Name and Clinic Number

Approval Date: **August 26, 2022**
Not to be used after: **August 25, 2023**

RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: Phase 1/2 Trial of Indomethacin in Chronic Pancreatitis (The PAIR Trial)

IRB#: 18-008193

Principal Investigator: Dr. Santhi Swaroop Vege and Colleagues

Key Study Information

This section provides a brief summary of the study. It is important for you to understand why the research is being done and what it will involve before you decide. **Please take the time to read the entire consent form carefully and talk to a member of the research team before making your decision.** You should not sign this form if you have any questions that have not been answered.	
It's Your Choice	This is a research study. Being in this research study is your choice; you do not have to participate. If you decide to join, you can still stop at any time. You should only participate if you want to do so. You will not lose any services, benefits or rights you would normally have if you choose not to take part.
Research Purpose	The purpose of this research is to find a way to slow down the progression of chronic pancreatitis (CP) and investigate the possibility of the long term treatment of this disease. You have been asked to take part in this research because you have been diagnosed with chronic pancreatitis.
What's Involved	Study participation will last 28 days, will be done in three visits, and will involve collection of blood, and saliva (at the beginning and the end), endoscopy procedures (at the beginning and the end) with pancreas juice collection, and taking daily study medications (indomethacin or placebo) for 28 days as well as completing data forms.

Key Information	Diagnostic Esophagogastroduodenoscopy (EGD) and Endoscopic Ultrasound (EUS) have a low (< 1%) risk of risk of complications, including reactions to medications given for sedation, bleeding, infection, pancreatitis, perforation, or urgent surgery for complications. There are no effective medical therapies for CP that alter the natural history of the disease. If indomethacin suppresses pancreatic PGE_2 production it may improve symptoms and delay progression of CP, but this would probably require long-term administration. Study participants will be patients with CP who will be receiving concurrent care for their condition as clinically appropriate and as determined by their treating physician.
Learn More	If you are interested in learning more about this study, read the rest of this form carefully. The information in this form will help you decide if you want to participate in this research or not. A member of our research team will talk with you about taking part in this study before you sign this form. If you have questions at any time, please ask us.

Making Your Decision

Taking part in research is your decision. Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you make your decision. Taking part in this study is completely voluntary and you do not have to participate.

If you decide to take part in this research study, you will sign this consent form to show that you want to take part. We will give you either a printed or electronic copy of this form to keep. A copy of this form will be put in your medical record.

For purposes of this form, Mayo Clinic refers to Mayo Clinic in Arizona, Florida and Rochester, Minnesota; Mayo Clinic Health System; and all owned and affiliated clinics, hospitals, and entities.

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Contact Information

If you have questions about …	You can contact …
▪ Study tests and procedures ▪ Materials you receive ▪ Research-related appointments ▪ Research-related concern or complaint ▪ Research-related injuries or emergencies ▪ Withdrawing from the research study	**Principal Investigator:** Dr. Santhi Vege **Phone:** (507) 266-9631 **Study Team Contact:** Vincent Anani or Graham Jaensch-Frie **Phone:** (507) 284-5660 **Institution Name and Address:** Mayo Clinic 200 First Street SW Rochester, MN 55905
▪ Rights of a research participant	**Mayo Clinic Institutional Review Board (IRB)** **Phone:** (507) 266-4000 **Toll-Free:** (866) 273-4681
▪ Rights of a research participant ▪ Any research-related concern or complaint ▪ Use of your Protected Health Information ▪ Stopping your authorization to use your Protected Health Information ▪ Withdrawing from the research study	**Research Participant Advocate (RPA)** **(The RPA is independent of the Study Team)** **Phone:** (507) 266-9372 **Toll-Free:** (866) 273-4681 **E-mail:** ResearchParticipantAdvocate@mayo.edu
▪ Billing or insurance related to this research study	**Patient Account Services** **Toll-Free:** (844) 217-9591

Other Information:

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.

Why are you being asked to take part in this research study?

You have been asked to take part in this research because you have been diagnosed with chronic pancreatitis. We estimate that there will be 32 participants in this study.

Why is this research study being done?

The purpose of this research is to find a way to slow down the progression of chronic pancreatitis (CP) and investigate the possibility of the long term treatment of this disease.

Information you should know

Who is Funding the Study?

This study is funded by a grant from the National Institute of Diabetes and Kidney Disorders (NIDDK).

Information Regarding Conflict of Interest:

Your healthcare provider may be referring you to this research study. If your healthcare provider is also an investigator on this study, there is the chance that his or her responsibilities for the study could influence his or her recommendation for your participation. If you prefer, your healthcare provider will be happy to refer you to another investigator on the research study team for you to decide if you want to participate in the study and to see you for the research study activities while you are in the study.

How long will you be in this research study?

Your participation in this study will last 28 days. You will receive a follow up phone call 30 days after your last study visit.

What will happen to you while you are in this research study?

If you want to take part in the study, we will ask you to sign this consent form before we do any study procedures.

This study uses a placebo. A placebo looks exactly like the study drug, but it contains no active ingredient. We use placebos in research studies to learn if the effects seen in research participants are truly from the study drug.

If you are eligible for the study, we will assign you by chance (like a coin toss) to the oral indomethacin 50 mg group or the placebo group. You and the Principal Investigator can't choose your study group. You will have an equal chance of being assigned to the indomethacin group or the placebo group. Neither you nor the Principal Investigator will know which study group you are in. However, in case of an emergency, this information will be available.

During this study, we will ask you to fill out questionnaires/complete diary about study medications, daily symptoms, and new or worsening symptoms or health concerns. We hope that you will answer all of the questions, but you can skip any questions you don't want to answer.

The study will consist of three in person visits with a follow-up phone call visit.

Visit 1:
At this time you will complete the baseline data forms and questionnaires and provide biological specimens (30 mL of blood and saliva).

Visit 2:
You will undergo EUS with ePFT (endoscopy with pancreas juice collection) at this visit. You will receive study medication at this time. Note: Urine pregnancy test will be done within 48 hours of the GI endoscopy. Also, if you have an EUS done for your care, pancreatic fluid will be collected during your clinical EUS. If you do not have a clinical EUS, then a research EUS with pancreatic fluid collection will be done for the study. All tests done just for research will paid for by the study. You are your insurance will be responsible for any tests done for your care (clinical).

For the next 28 days following endoscopy procedure, you will be asked to take study medication twice daily and complete study diary daily. A study team member will call you weekly by telephone to complete data forms.

Visit 3:
At this visit you complete data forms and questionnaires, provide biological specimens (20 mL of blood and saliva), undergo EUS with ePFT (an endoscopy with pancreas juice collection).

Follow up telephone visit:
A study team member will contact you by telephone to complete a data form.

Tests done only for research purposes are not meant to provide clinical information or help care for you. The results are only important for research. Therefore, the results of tests done with your information and samples will not be provided to you. In the rare event that a finding might affect the health of you or your family, we will contact you and you can choose whether to receive or refuse the information. If you decide to follow up and further medical testing or care is needed, the costs will be billed to you or your insurance.

What are the possible risks or discomforts from being in this research study?

Endoscopy, EUS, and ePFT: Upper GI endoscopy (EGD) and endoscopic ultrasound (EUS) are routine clinical diagnostic procedures that are typically performed under conscious sedation or monitored anesthesia care. Diagnostic EGD and EUS have a low (< 1%) risk of risk of complications, including reactions to medications given for sedation, bleeding, infection, pancreatitis, perforation, or urgent surgery for complications. All study participants will be undergoing a baseline clinically indicated EGD or EUS exam as well as a subsequent research EGD exam, with endoscopic pancreatic function tests (ePFTs) during both exams.

ePFT is performed during EGD and EUS and involves administration of intravenous secretin. ePFT lengthens the duration of an endoscopic exam because pancreas juice is collected from the duodenum via the endoscope for 45 minutes after secretin administration. There is no evidence that performance of ePFT increases the overall risks of EGD or EUS.

Side effects of intravenous secretin administration occur in < 1% and include diaphoresis, hypotension, nausea, abdominal pain, vomiting, mild pancreatitis, upset stomach, diarrhea, flushing, and a warm sensation in the abdomen.

Indomethacin (IN) is a nonsteroidal anti-inflammatory drug (NSAID), and many drugs in this class are available over-the-counter. IN was chosen for use in this study because rectally administered IN is known to have a beneficial anti-inflammatory effect in human pancreas for prevention of post-ERCP pancreatitis. Like other NSAIDs, IN has a low risk of complications, including allergic reactions, gastrointestinal ulceration, GI bleeding, and a small increased risk of vascular events such as stroke or myocardial infarction. Patients with a history of allergy to NSAIDS, current or past gastroduodenal ulceration, or past history of stroke, myocardial infarction, or coronary artery disease are excluded from participation in this study.

Women who are pregnant or nursing: Risks of endoscopy and sedation may be increased in women who are pregnant or nursing, and they are excluded from participation in this study.

Women of child-bearing potential will undergo a urine pregnancy test within 48 hours of their research EGD exam. In addition, at the time of enrollment they must agree to one of the following birth control methods:

- Hormonal methods, such as birth control pills, patches, injections, vaginal ring, or implants
- Barrier methods (such as a condom or diaphragm) used with a spermicide (a foam, cream, or gel that kills sperm)
- Intrauterine device (IUD)
- Abstinence (no sex)

They must use birth control for the entire study and for at least 5 days after their last dose of study drug.

Pregnancy
Indomethacin may cause premature closure of the ductus arteriosus in a fetus. Avoid use of NSAIDs, including indomethacin capsules, in pregnant women starting at 30 weeks gestation (third trimester).

Psychological, legal and financial risks: Study questionnaires will collect confidential information, including medical history, medications used, pain ratings, and quality of life information. Public release of this information might have adverse consequences for study participants. All study data will therefore be stored in secure paper files or de-identified, password-protected electronic databases.

Are there reasons you might leave this research study early?

You may decide to stop at any time. You should tell the Principal Investigator if you decide to stop, and you will be advised whether any additional tests may need to be done for your safety.

In addition, the Principal Investigator, the study sponsor or Mayo Clinic may stop you from taking part in this study at any time:

- If it is in your best interest,
- If you don't follow the study procedures,
- If the study is stopped.

If you leave this research study early, or are withdrawn from the study, no more information about you will be collected; however, information already collected about you in the study may continue to be used.

We will tell you about any new information that may affect your willingness to stay in the research study.

What if you are injured from your participation in this research study?

Where to get help:
If you think you have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the beginning of this form. Mayo Clinic will offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

Who will pay for the treatment of research related injuries?
Care for such research-related injuries will be billed in the ordinary manner, to you and your insurance. Treatment cost for research-related injuries not covered by your insurance will be paid by Mayo Clinic.

What are the possible benefits from being in this research study?

Subjects are unlikely to benefit from participation in this study. If indomethacin suppresses pancreatic PGE_2 production it may improve symptoms and delay progression of CP, but this would probably require long-term administration. Others with CP may benefit in the future from what we learn in this research study.

What alternative do you have if you choose not to participate in this research study?

There are no effective medical therapies for CP that alter the natural history of the disease. Study participants will be patients with CP who will be receiving concurrent care for their condition as clinically appropriate and as determined by their treating physician.

What tests or procedures will you need to pay for if you take part in this research study?

You won't need to pay for tests and study assessments which are done for research purpose only. These are:

- Endoscopy with pancreas juice collection performed only for research purposes
- Study medication provided only for research purposes
- Collection of biospecimens (blood and saliva) for research purposes

However, you and/or your insurance will need to pay for all other tests and procedures that you would have as part of your clinical care.

If you have billing or insurance questions call Patient Account Services at the telephone number provided in the "Contact Information" section of this form.

Will you be paid for taking part in this research study?

Participants who complete the study protocol, including 28 days of study medication and follow-up endoscopy with pancreas juice collection, will be paid $250 remuneration, and up to an additional $250 reimbursement for travel expenses including mileage, parking, hotel and airfare. In order to receive reimbursement, you must provide a copy of the original receipts for those expenses.

Participants who complete the first pancreatic juice collection but who do not complete the entire protocol will receive $50 remuneration and no additional reimbursement. Payments will be made by check which will be mailed to you (participants who are Mayo employees will receive remuneration in their paycheck).

Participants who do not complete the first pancreatic juice collection will not receive remuneration or reimbursement.

Sometimes, research results in findings or inventions that have value if they are made or sold. These findings or inventions may be patented or licensed, which could give a company the sole right to make and sell products or offer testing based on the discovery.

Some of the profits from this may be paid back to the researchers and the organizations doing this study, but you will not receive any financial benefits.

Payment for participation in research is considered taxable income and reportable to the Internal Revenue Service (IRS). Accounts Payable at Mayo Clinic will be given your name, address and Social Security number in order to issue a check for your study participation. If you receive research payments totaling $600 or more in a calendar year, a tax Form 1099 will be sent to you. For Mayo Clinic employees, research payments are included in your paycheck with applicable taxes withheld and reported on your Form W2 after calendar year-end.

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Will your information or samples be used for future research?

Your samples will be used for research purposes as described in this form. If you agree, your samples may also be used for future research into pancreatitis, pancreatic cancer, or other medical diseases, and genetic analysis may be performed using your specimens. Mayo Clinic may destroy the samples at any time without telling you. Mayo Clinic may keep your samples indefinitely.

In the future your samples may be sent to a central biospecimen repository not located at Mayo Clinic. Other researchers at Mayo Clinic and other institutions who aren't involved with this study may be given access to your samples for future studies. Your sample will be sent to a central biospecimen repository or other researchers in a coded format, which protects your identity. However, once we release your coded data to the central research database we are no longer in control of the information.

Some future studies may examine your DNA, which is the genetic information you inherited from your parents (genetic testing). The Principal Investigator may contact you if there are findings which may be useful for your health care. You would be given general information on the potential risks, benefits, and costs of choosing to learn about the findings. There is a very small chance that some commercial value may result from the use of your donated sample. If that happens, you won't be offered a share in any profits.

In order for your specimens to be used for future research you must give permission to share your specimen. Please read the section below and think about whether you are willing to do this. Please check the answers that are right for you. If you have any questions, please talk to your doctor or nurse.

1. I consent to the use of my biological samples for any future research:

   ☐ Yes ☐ No Please initial here: _____Date: _____

2. I consent to the use of my biological samples for Genetic Analysis for any future research:

   ☐ Yes ☐ No Please initial here: _____Date: _____

3. I consent to the authorization of future contact for research purposes:

☐ Yes ☐ No Please initial here: _____Date: _____

You may withdraw your consent for future use of your information and/or samples at any time, by writing to the Principal Investigator at the address provided in the "Contact Information" section of this consent form.

Your information and/or samples would be removed from any repository where they are stored, if possible. Information and/or samples already distributed for research use will not be retrieved.

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information when making a decision to hire, promote, or fire you or when setting the terms of your employment.

All health insurance companies and group health plans must follow this law.

Be aware that this new Federal law doesn't protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

How will your privacy and the confidentiality of your records be protected?

Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study.

Mayo Clinic policies and certain federal and state laws require that personal health information be kept confidential but allow disclosures in specific situations. You will be informed of these confidentiality policies and laws that apply to this study and you will also be asked to sign an authorization to permit the researchers in this study to obtain access to, use and disclose your personal health information in this study as described in this consent form.

There are many reasons why your health information may be used or disclosed in the course of this study. For example, the researchers may need the information to verify that you are eligible to participate in the study, or to monitor the results, including side effects. Other university and government officials, safety monitors, and study sponsors may need the information to ensure that the study is conducted properly. Also, information may need to be disclosed to insurance companies or others responsible for your medical bills in order to secure payment.

All the data will be recorded in data sheets and your medical records and then entered into a password protected database. We shall keep your records confidential, to the extent provided by federal, state and local law. We shall not allow anyone to see your record, other than people who have a right to see it (i.e., principal investigator, co-investigators, etc.). You will not be identified in any reports on this study.

During this research, information about your health will be collected. Under Federal law called the Privacy Rule, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use and share your health information for research and why they may need to do so. Information about you and your health cannot be used in this research study without your written permission. If you sign this form, it will provide that permission (or "authorization") to Mayo Clinic.

Your health information may be collected from:

- Past, present and future medical records.
- Research procedures, including research office visits, tests, interviews and questionnaires.

Your health information will be used and/or given to others to:

- Do the research.
- Report the results.
- See if the research was conducted following the approved study plan, and applicable rules and regulations.

Your health information may be used and shared with:

- Mayo Clinic research staff involved in this study.
- Other Mayo Clinic staff involved in your clinical care.
- Researchers involved in this study at other institutions.
- The sponsor(s) of this study and the people or groups hired by the sponsor(s) to help perform this research.
- The Mayo Clinic Institutional Review Board that oversees the research.

- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health and other United States agencies) or government agencies in other countries that oversee or review research.
- A group that oversees the data (study information) and safety of this research.

How your information may be shared with others:

While taking part in this study, you will be assigned a code that is unique to you but does not include information that directly identifies you. This code will be used if your study information is sent outside of Mayo Clinic. The groups or individuals who receive your coded information will use it only for the purposes described in this consent form.

If the results of this study are made public (for example, through scientific meetings, reports or media), information that identifies you will not be used.

In addition, individuals involved in study oversight and not employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site location). These records contain information that directly identifies you. However, the individuals will not be allowed to record, print, copy (using paper, digital, photographic or other methods), or remove your identifying information from Mayo Clinic.

Is your health information protected after it has been shared with others?

Mayo Clinic asks anyone who receives your health information from us to protect your privacy; however, once your information is shared outside Mayo Clinic, we cannot promise that it will remain private, and it may no longer be protected by the Privacy Rule.

Your Rights and Permissions

Participation in this study is completely voluntary. You have the right not to participate at all. Even if you decide to be part of the study now, you may change your mind and stop at any time. You do not have to sign this form, but if you do not, you cannot take part in this research study.

Deciding not to participate or choosing to leave the study will not result in any penalty. Saying 'no' will not harm your relationship with your own doctors or with Mayo Clinic.

If you cancel your permission for Mayo Clinic to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.

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You can cancel your permission for Mayo Clinic to use or share your health information at any time by sending a letter to the address below:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
201 Building 4-60
200 1st Street SW
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Participant Advocate at: ResearchParticipantAdvocate@mayo.edu.

Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number and /or study name, and
- Your contact information.

Your permission for Mayo Clinic to use and share your health information lasts forever, unless you cancel it.

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Enrollment and Permission Signatures

Your signature documents your permission to take part in this research.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature

Person Obtaining Consent

- I have explained the research study to the participant.
- I have answered all questions about this research study to the best of my ability.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature