University of Illinois at Chicago
Research Information and Consent for Participation in Biomedical Research
Lidocaine Infusion in Pancreatic Cancer: Translational Studies in a Preclinical Model And Human Subjects

You are being asked to participate in a research study. Researchers are required to provide a consent form such as this one to tell you about the research, to explain that taking part is voluntary, to describe the risks and benefits of participation, and to help you to make an informed decision. You should feel free to ask the researchers any questions you may have.

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Emergency Contact Name and Information: Call (312) 996-7000 and request to speak to the anesthesiology Pain Resident on call or Dr. Votta-Velis (312-996-4020), or dial 911.

Sponsor: American Society of Regional Anesthesia and Pain Medicine Carl Koller Memorial Research Grant

Why am I being asked?

You are invited to take part in this study because you have a cancer of the pancreas and are scheduled for surgery to remove the cancer. You need to understand the risks and benefits to make a decision about whether or not to be in this study.

This form is called a consent form. The intent of this form is to let you know the purpose of this study, the treatment plan, and the possible risks and benefits of participation. If you wish to take part in this study, you will be asked to sign this consent form. Research studies only include people who want to take part. Please take time to make your decision. We encourage you to discuss your decision with your doctors, family, and friends.

This research study is being conducted in the Department of Surgery and the Department of Anesthesiology at the University of Illinois at Chicago. Gina Votta-Velis, M.D. is the principal investigator (the physician in charge) of this research study.

Your health care provider may be an investigator on this research protocol, 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 a clinician who is not associated with this project. You are not obligated to participate in any research project offered by your clinician. Your participation in this research study is voluntary and you do not have to participate. The decision to not participate will not affect your clinical care now or in the future.

Your participation in this research is voluntary. Your decision whether or not to participate will not affect your current or future dealings with the University of Illinois at Chicago. **If you decide to participate, you are free to withdraw at any time without affecting that relationship.**

Approximately 46 subjects may be involved in this research at UIC.

What is the purpose of this research?

The purpose of this study is to collect information on whether lidocaine, a local anesthetic, drug, reduces activation of a protein, Src tyrosine protein kinase (or Src for short) within Circulating Tumor Cells during or after pancreatic surgery. Circulating Tumor Cells are cells that come from tumors and enter into the bloodstream and can cause metastasis. You may have Circulating Tumor Cells in your bloodstream because of your pancreatic cancer. When you have your pancreas removed we are interested in determining 1) if the surgical procedure itself increases Circulating Tumor Cells levels in your bloodstream, 2) whether Src activity is increased in those Circulating Tumor Cells, and 3) if so, whether lidocaine decreases Src activity. Src activation is thought to be responsible in part for cancer metastases (your cancer spreading to other sites in your body). There are preclinical studies (studies done in cancer cells and animals in the laboratory) that indicate that local anesthetics decrease Src activation. There will be two groups in this study and which group you will be assigned to will be determined by a random process (for example, by a flip of a coin). One group of patients will receive a lidocaine infusion immediately before, during, and after the surgical procedure (total duration of infusion: 24 hours). The other group will receive a saline (salt water, or placebo) infusion immediately before, during, and after the surgical operation (total duration of infusion: 24 hours). We will be taking blood samples from you at different times - before, during and after your operation. We will also be drawing additional blood to measure several substances in your blood including cytokines and VEGF (vascular endothelial growth factor). Cytokines are compounds made by the body as part of its immune function. A cytokine is produced by certain cells when they come into contact with threatening substances in the body such as bacteria. VEGF can cause tumor cells to be released from blood vessels to the outside of the vessels onto tissues where they can grow (process called metastasis or spread of tumors). Cytokines and VEGF are often released when tissues in your body are injured, such as during major surgery, including removal of the pancreas. We will examine whether lidocaine has any effect on levels of these substances in the

bloodstream by comparing levels in the patients receiving lidocaine and levels in the patients receiving saline (that is, placebo).

Once your pancreatic tumor is removed, tissue samples will be taken from it so that we can determine level of Src activity in the tumor and compare it to level of Src activity in your blood samples.

What procedures are involved?

If you consent to participate, your participation in this study involves the following:

In the preoperative holding area after you are sedated, we will insert a catheter into an upper extremity vein (for example, a vein in your forearm). Once you are in the operating room, we will use this catheter to administer the lidocaine infusion or the saline infusion through a pump. We will be taking blood samples from you on four separate occasions to measure Circulating Tumor Cells, Src activity within those cells, and cytokines and VEGF: before the pump is turned on, during the removal of your pancreas, and 24 hours, and 72 hours after the start of the lidocaine or saline infusion. Blood will be drawn from an upper-extremity vein each time we take a sample from you. In addition, a blood sample will be obtained from your portal vein (a vein leading to your liver) once during the surgery. The amount of blood we will draw from you at each sampling time is shown in the table below, expressed in milliliters as well as teaspoons. The total amount of blood to be drawn during the study is about 14 2/3 teaspoons or 72 milliliters.

Blood Sample Collection Time	Amount of blood drawn in milliliters (or teaspoons [tsp])
Before infusion	16 milliliters (3 1/3 tsp)
During surgery	24 milliliters (4 1/2 tsp)
24 hours after start of infusion	16 milliliters (3 1/3 tsp)
72 hours after start of infusion	16 milliliters (3 1/3 tsp)

What are the potential risks and discomforts?

The risks of taking blood include pain, a bruise at the point where the blood is taken, redness and swelling of the vein and infection, and a rare risk of fainting.

You may or may not receive a lidocaine infusion as part of this research study. The potential side effects of lidocaine are listed below.

More likely:

- feeling lightheaded,
- shaking,
- low blood pressure,

- drowsiness,
- confusion,
- weakness,
- blurry or double vision,
- dizziness

Less likely:

- **Lidocaine toxicity**. This occurs with doses much higher (5-10 times higher) than the dose that will be tested in this study. However, lidocaine toxicity has never been reported in such low rates of infusion. Lidocaine toxicity includes:
  - Changes in heart rate and blood pressure as well as a possibility of a heart attack.
  - Nervous system effects including seizures
  - Gastrointestinal effects including nausea and vomiting
  - Hypersensitivity (allergic reactions) including anaphylaxis (severe allergic reaction), adult respiratory distress syndrome (ARDS), and loss of blood flow to brain, heart and other organs and that have occasionally resulted in death
  - Psychiatric reactions including transient (not permanent) mental disorders that lead to impairment of emotions and thoughts.
  - Effects on different organs of the body limited to rare reports of decreased delivery of oxygen to the tissues. **Risk of loss of confidentiality:** There is the risk for the potential loss of confidentiality. This means that the risk of release of private information from their health records can occur. Release of this private information might affect the subjects in the future. We believe the chance this will happen is very small, but we cannot make guarantees. Your privacy and the confidentiality of your data are very important to us and we will make every effort to protect them. These efforts are described in the section below called "What about privacy and confidentiality?".

For more information about risks and side effects, ask your study doctor.

Will I be told about new information that may affect my decision to participate?

During the course of the study, you will be informed of any new findings (either good or bad), such as changes in the risks or benefits resulting from participation in the research or new alternatives to participation, that might cause you to change your mind about continuing in the study. If new information is provided to you, your consent to continue participating in this study may be re-obtained.

Are there benefits to taking part in the research?

This study is not being done to improve your condition or health. It is hoped that knowledge gained from this research may benefit you and others with cancer in the future

What other options are there?

You have the option to not participate in this study.

What about privacy and confidentiality?

Will health information about you be created, used or shared with others during this study? State and federal laws, including the Health Insurance Portability and Accountability Act (HIPAA), require researchers to protect your health information. This section of this form describes how researchers, with your authorization (permission), may use and release (disclose or share) your protected health information in this research study. By signing this form you are authorizing Dr. Gina Votta-Velis and her research staff or team, to create, get, use, store, and share protected health information that identifies you for the purposes of this research.

The health information includes all information created and/or collected during the research as described within this consent form and/or any health information in your medical record that is needed for the research and that specifically includes demographic, clinical, and laboratory variables. Demographic variables will include subject sex, birth date, race/ethnicity, and height and weight. Clinical variables will include current diagnoses, date and duration of surgery, opioid consumption during and after surgery, histology, and tumor grade. Laboratory values will include Src kinases activity, adhesion molecules, CTC number, and plasma levels of cytokines and other proteins, a single cell RNA sequencing and silencing of specific genes in isolated CTCs.

During the conduct of the research, the researchers may use or share your health information:

- With each other and with other researchers involved with the study;
- With law enforcement or other agencies, when required by law;
- With the sponsor/funding agency of the research, American Society of Regional Anesthesia and Pain Medicine, as required to conduct the research and if the research results need to be confirmed;
- With representatives of government agencies (i.e., Food and Drug Administration), review boards including the University of Illinois at Chicago Institutional Review Board, the University of Illinois Medical Center and its representatives, and other persons who watch over the safety, effectiveness, and conduct of research.

Therefore, the de-identified information may be used and released by the researchers (as permitted by law) for other purposes, such as other research projects.

You will not have access to the health information related to this research study until the study is done. However, this information is available to your doctor in the case of an emergency. At the end of the study, you will again have access to health information that is normally within your

medical records (treatment, insurance and billing information). However, the researcher may not give you access to the research records or information that is not usually kept in your medical record, as it is not required by HIPAA.
The people who will know that you are a research subject are members of the research team, and if appropriate, your physicians and nurses. No information about you, or provided by you, during the research, will be disclosed to others without your written permission, except if necessary to protect your rights or welfare (for example, if you are injured and need emergency care or when the UIC Office for the Protection of Research Subjects monitors the research or consent process) or if required by law.

The records of this study will be kept private. Information will be kept in your medical record and in study case report forms. Your blood and tumor tissue samples will not be labeled with your name on them; instead, the samples will be labeled with a unique coded subject study number. Information gained from this study will be used for research and educational purposes. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

To this extent, confidentiality is not absolutely guaranteed.

If you decide to participate in this study, some private health information about you will be stored in a computer database at the University of Illinois department of Anesthesiology. This information will include your name and medical record number, date of birth, diagnosis, race/ethnicity, and information about your participation in this study. The purpose of storing this information is to assist the investigators in creating reports about research and in making sure that research studies are being done correctly. Your information will not be used for any other purpose. We will store your information for 6 years after the research is finished and then erase it.

How will your health information be protected?

The researchers and American Society of Regional Anesthesia and Pain Medicine agree to protect your health information and will only share this information as described within this research consent/authorization form.

When your health information is given to people outside of the research study, those agencies that receive your health information may not be required by federal privacy laws (such as the Privacy Rule) to protect it. They may also share your information with others without your permission, if permitted by laws that they have to follow.

Protected Health Information (PHI)

Your PHI created or received for the purposes of this study is protected under the federal regulation known as HIPAA. Refer to the attached HIPAA authorization for details concerning the use of this information.

A possible risk of the research is that your participation in the research or information about you and your health might become known to individuals outside the research.

When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity.

What if I am injured as a result of my participation?

You may have medical problems or side effects from taking part in this research study. If you believe that you have become ill or been injured from taking part in this study, treatment may be obtained through:

- UI Health OR
- Your regular doctor OR
- The treatment center or clinic of your choice.

If you do seek medical treatment, please take a copy of this document with you because it may help the doctors where you seek treatment. It will also provide the doctors where you seek treatment with information they may need if they want to contact the research doctors.

You may contact the researcher Dr. Gina Votta-Velis at (312) 996-4020 to talk to her about your illness or injury. In the case of an emergency, you may call (312) 996-7000 and enter pager #7978 to speak to the anesthesiology Pain Physician on call. If it is a true medical emergency, contact 911 and seek emergency medical attention before contacting the investigator.

You or your insurance company will be billed for this medical care (that is, your pancreatic surgery and after-care). Your insurance company may not pay for some or all of this medical care because you are participating in a research study. There are no plans for the University to provide free medical care or to pay for research-related illnesses or injuries, or for the University to provide other forms of compensation (such as lost wages or pain and suffering) to you for research related illnesses or injuries.

By signing this form you will not give up any legal rights.

What are the costs for participating in this research?

You will not be charged for costs of the lidocaine and/ or saline infusions or the processing of blood samples for research purposes. The cost of the lidocaine and/or of the saline infusions and the costs of collecting and processing of the research related blood samples will be covered by the study investigators.

All the other costs associated with the standard medical and surgical care of pancreatic cancer will be charged to you and/or your health insurance/health plan. You also will be responsible for any co-payments and deductibles.

Will I be reimbursed for any of my expenses or paid for my participation in this research?

You will receive no payment or compensation for taking part in this study.

Can I withdraw or be removed from the study?

Your Authorization for release of health information for this research study expires 6 year after the end of the study, but can be canceled sooner if you decide to withdraw your permission.

You may change your mind and cancel this Authorization at any time. To cancel this Authorization, you must write to: ginavot@uic.edu.

If you cancel this Authorization, you may no longer be allowed to take part in the research study. Even if you cancel this Authorization, the researchers may still use and disclose health information they have already obtained as necessary to maintain the integrity and reliability of the research and to report any adverse (bad) effects that may have happened to you.

If you decide to participate, you are free to withdraw your consent and discontinue participation at any time without affecting your future care at UI Health.

You have the right to leave a study at any time without penalty. For your safety, however, you should consider the investigator's advice about how to leave the study.

The researchers and sponsor also have the right to stop your participation in this study without your consent if:

- They believe it is in your best interests;
- You do not follow the study requirements; or
- The study is stopped for any reason.

No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

What if I am a UIC student?

You may choose not to participate or to stop your participation in this research at any time. This will not affect your class standing or grades at UIC. The investigator may also end your participation in the research. If this happens, your class standing or grades will not be affected. You will not be offered or receive any special consideration if you participate in this research.

What if I am a UIC employee?
Your participation in this research is in no way a part of your university duties, and your refusal to participate will not in any way affect your employment with the university, or the benefits, privileges, or opportunities associated with your employment at UIC. You will not be offered or receive any special consideration if you participate in this research.

Who should I contact if I have questions?

Contact the researcher Dr. Gina Votta-Velis at (312) 996-4020 or email address ginavot@uic.edu:

- 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 treatment), and/or
- if you have questions, concerns or complaints about the research.

What are my rights as a research subject?

If you have questions or concerns regarding your privacy rights under HIPAA, you should contact the University of Illinois at Chicago Privacy Officer at Ph: (312) 996-2271.

Right to Refuse to Sign this Authorization
You do not have to sign this Consent/Authorization. However, because your health information is required for research participation, you cannot be in this research study if you do not sign this form. If you decide not to sign this Consent/Authorization form, it will only mean you cannot take part in this research. Not signing this form will not affect your non-research related treatment, payment or enrollment in any health plans or your eligibility for other medical benefits.

If you have questions about your rights as a research subject or concerns, complaints, or to offer input you may call the Office for the Protection of Research Subjects (OPRS) at 312-996-1711 or 1-866-789-6215 (toll-free) or e-mail OPRS at uicirb@uic.edu.

Remember:

Your participation in this research is voluntary. Your decision whether or not to participate will not affect your current or future relations with the University of Illinois. If you decide to participate, you are free to withdraw at any time without affecting that relationship.

Signature of Subject

I have read (or someone has read to me) the above information. I have been given an opportunity to ask questions and my questions have been answered to my satisfaction. I agree to participate in this research. I will be given a copy of this signed and dated form.

If you have not already received a copy of the Notice of Privacy Practices, you should ask for one.

Your signature below indicates that you are providing both consent to participate in the research study and authorization for the researcher to use and share your health information for the research.

_____	_____
Signature	Date
_____	
Printed Name	
_____	_____
Signature of Person Obtaining Consent	Date (must be same as subject's)
_____	
Printed Name of Person Obtaining Consent	