COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT

YALE UNIVERSITY SCHOOL OF MEDICINE – YALE-NEW HAVEN HOSPITAL

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Study Title: PHASE II STUDY OF PERI-OPERATIVE MODIFIED FOLFIRINOX IN LOCALIZED PANCREATIC CANCER

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Funding Source: Yale Comprehensive Cancer Center

INVITATION TO PARTICIPATE AND DESCRIPTION OF PROJECT

You are invited to take part in a research study designed to look at the effectiveness of a combination of four chemotherapy drugs in the treatment of localized non-metastatic pancreatic cancer that can be surgically removed. This combination of four drugs is called FOLFIRINOX. You have been invited to take part because you have localized pancreatic cancer.

We are conducting this study to see whether the FOLFIRINOX treatment administered to patients with localized pancreatic cancer that can be removed surgically is as good as or better than the currently available treatment for localized pancreatic cancer. Based on the potential advantages of administration of chemotherapy before surgery in patients with localized pancreatic cancer, we propose treating patients with FOLFIRINOX both before and after surgery. We will use reduced doses of two of the drugs in the FOLFIRINOX regimen (bolus 5-fluorouracil and irinotecan), which may be associated with improved tolerability compared to full dose FOLFIRINOX.

In order to decide whether or not you wish to be a part of this research study you should know enough about its risks and benefits to make an informed decision. This consent form gives you detailed information about the study, which a member of the research team will discuss with you. This discussion should go over all aspects of this research: the purpose and nature of the research, the procedures that will be performed, the risks of the study drugs and procedures, possible benefits, possible alternative treatments, your rights as a participant and other information about the research study. You should take whatever time you need to discuss the research study with your physician and family. The decision to participate or not is yours. Once you understand the study, you will be asked if you wish to participate; if so, you will be asked to sign and date where indicated on this form.

If you choose to participate, you will be told of any significant new findings that develop during the course of your participation in this study that may affect your willingness to continue to participate.

The research study is being funded by Yale Comprehensive Cancer Center. Yale Comprehensive Cancer Center is providing research support and study drug for this research study. Dr. Jill Lacy is the principal investigator of this study at Yale Comprehensive Cancer Center.

PURPOSE:

The purpose of this study is to test the effectiveness and safety of a modification of the FOLFIRINOX chemotherapy regimen in patients with localized pancreatic cancer who are eligible for surgical removal of their tumor.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

Approximately 46 subjects will be enrolled to take part in this study. This study is only being done at the Yale Comprehensive Cancer Center.

STUDY PROCEDURES

Screening Period:

If you agree to participate and sign and date this form, you will need to undergo a series of tests and procedures to determine if you are eligible to participate in the research study. You will come to the study site for screening tests and it is possible that more than one screening visit may be needed. The following tests or procedures will be performed during the visit(s):

Within 14 days of starting study drugs:

- You will have a surgical evaluation
- A review of your medical history and the medications you are currently taking or have recently taken
- Review of any adverse events you are experiencing
- A physical examination, measurement of vital signs (including height, weight, temperature, heart rate and blood pressure) and an evaluation of your performance status
- 1-2 tablespoons (or 15-30 milliliters) of blood will be collected for routine laboratory tests to see if you are eligible to receive the study drugs
- Blood will be collected to test your CA19-9 and CEA levels.
- A pregnancy test (if you are female and of childbearing potential)
- An optional blood sample (30 milliliters) will be drawn for research purposes. You will be asked to indicate whether or not you agree to this sample at the end of this form. The choice to provide this sample is up to you. If you choose not to provide the sample, you can still participate in this study.

Within 21 days of starting study drugs:

- Imaging studies to assess and measure your disease, which will include CT (computed tomography) scan or MRI (magnetic resonance imaging) and a PET (positron emission tomography) scan.

Within 42 days of starting study drugs:

- Endoscopic Ultrasound

You will be evaluated based on the results of these tests in order to determine if you are eligible to participate in this study. If your physician finds that you are not eligible, then you will not receive treatment as part of this research study.

What will happen if I take part in this research study?

If you agree to participate in this study, and the exams, tests, and procedures show that you meet the criteria to be in the study, then you will receive chemotherapy treatment before surgery with the modified FOLFIRINOX regimen (called mFOLFIRINOX). Everyone in this study will get the same chemotherapy drugs. This is a combination of four drugs: 5-fluouracil, oxaliplatin, levoleucovorin and irinotecan. These drugs will be given to you in the infusion center at Smilow Cancer Hospital. All drugs are given into the vein, through a Port-a-cath which is a catheter that goes into the vein with an access port under the skin.

You will begin study drugs within 14 days of signing up for this trial. Prior to surgery, you will receive mFOLFIRINOX intravenously every 2 weeks. One cycle is 2 weeks. After completion of 6 cycles, you will undergo re-assessment before cancer surgery. If you are deemed as a surgical candidate, you will undergo surgery to remove the tumor in your pancreas within 3-8 weeks of completion of 6 cycles of neoadjuvant mFOLFIRINOX. Neoadjuvant means before your surgery.

You will continue to be seen every 2 weeks (or every cycle) by your study doctor after your surgery to assess readiness to start adjuvant (supplemental) therapy.

After surgery, you will receive an additional 6 cycles of mFOLFIRINOX. The post-operative chemotherapy with mFOLFIRINOX will start when you have sufficiently recovered from your surgery, have no open incisions, have normalization of laboratory tests, and have demonstrated stable or increasing weight for more than one week. The post-operative chemotherapy will be started within 12 weeks of surgery.

The following is a list of evaluations that you will undergo during the treatment period of the study:

Day 1 of each cycle:

- A review of your medical history and the medications you are currently taking or have recently taken
- Review of any adverse events you are experiencing or have experienced since your last visit

- A physical examination, measurement of vital signs (including weight, temperature, heart rate and blood pressure) and an evaluation of your performance status
- 1-2 tablespoons (or 15-30 milliliters) of blood will be collected for routine laboratory tests to see if you are eligible to receive treatment on that day. Medication to prevent nausea will be given by mouth and also injected into your vein through the port-a-cath.
- After you have received the medications for nausea, the first drug, oxaliplatin, will be injected into your vein through the port-a-cath for 2 hours. If your study doctor determines it is necessary, you will be given salts of calcium and magnesium injected into your vein for about 15 minutes just before and just after receiving the oxaliplatin.
- After the oxaliplatin, the second and third drugs, levoleucovorin and irinotecan, will be injected at the same time through the port-a-cath for 2 hours.
- After the levoleucovorin and irinotecan, the fourth drug, fluorouracil, will be injected over 15 minutes.
- The fourth drug, fluorouracil, will be placed into an infusion pump that is connected to the port-a-cath. The fluorouracil will then be infused or dripped into your vein through the port-a-cath over the next 46 hours after you leave the clinic, while you are at home. After the 46 hour period of chemotherapy infusion, the pump will be disconnected from the port-a-cath and the chemotherapy treatment is completed. You may return to the clinic to have the pump disconnected or arrangements will be made to have the pump disconnected at your home.

Day 3, 4, or 5 of each cycle:

- You will return to the clinic to get an injection with a drug called Neulasta. This is given under the skin and is used to help increase your white blood cell count – these are the cells that fight infection. Chemotherapy decreases the number of these cells, and Neulasta is used to help your body to produce more of these cells more quickly.

Day 8 of Each Cycle:

- You will have a blood test. One tablespoon (or 15 milliliters) of blood will be collected to monitor the effect of the chemotherapy on your blood counts and blood chemistry.

On Day 8 of Cycle 1 only, you will also have the following done:

- A physical examination, measurement of vital signs (including weight, temperature, heart rate and blood pressure) and an evaluation of your performance status
- Review of any adverse events you are experiencing or have experienced since your last visit

Within 4 weeks of your surgery (unless otherwise indicated):

- You will have a surgical evaluation
- 1-2 tablespoons (or 15-30 milliliters) of blood will be collected for routine laboratory tests

- You will undergo a PET scan after the third cycle of mFOLFIRINOX and within one week of starting cycle 4.
- An optional blood sample (10-20 milliliters) will be drawn for research purposes. You will be asked to indicate whether or not you agree to this sample at the end of this form. The choice to provide this sample is up to you. If you choose not to provide the sample, you can still participate in this study. This sample will be drawn after cycle 6 and within 3-8 weeks of your surgery.

Day 1 of Cycle 7 (within 12 weeks of your surgery)

- A review of your medical history and the medications you are currently taking or have recently taken
- Review of any adverse events you are experiencing and have experienced since your last visit
- A physical examination, measurement of vital signs (including weight, temperature, heart rate and blood pressure) and an evaluation of your performance status
- 1-2 tablespoons (or 15-30 milliliters) of blood will be collected for routine laboratory tests to see if you are eligible to receive treatment on that day
- Blood will be collected to test your CA19-9 and CEA levels
- An optional blood sample (10-20 milliliters) will be drawn for research purposes. You will be asked to indicate whether or not you agree to this sample at the end of this form. The choice to provide this sample is up to you. If you choose not to provide the sample, you can still participate in this study.
- Medications to prevent nausea will be given by mouth and also injected into your vein through the port-a-cath.
- After you have received the medications for nausea, the first drug, oxaliplatin, will be injected into your vein through the port-a-cath for 2 hours. If your study doctor determines it is necessary, you will be given salts of calcium and magnesium injected into your vein for about 15 minutes just before and just after receiving the oxaliplatin.
- After the oxaliplatin, the second and third drugs, levoleucovorin and irinotecan, will be injected at the same time through the port-a-cath for 2 hours.
- After the levoleucovorin and irinotecan, the fourth drug, fluorouracil, will be injected over 15 minutes.
- The fourth drug, fluorouracil, will be placed into an infusion pump that is connected to the port-a-cath. The fluorouracil will then be infused or dripped into your vein through the port-a-cath over the next 46 hours after you leave the clinic, while you are at home. After the 46 hour period of chemotherapy infusion, the pump will be disconnected from the port-a-cath and the chemotherapy treatment is completed. You may return to the clinic to have the pump disconnected or arrangements will be made to have the pump disconnected at your home.

You will have a CT scan, or MRI performed after the first six cycles of mFOLFIRINOX prior to undergoing surgery, and again after completion of all cycles of mFOLFIRINOX (12 cycles in total) . You will remain on study until your disease worsens, you experience unacceptable toxicity or your study doctor determines that you are no longer benefiting from the study.

How long will I be in the study?

If your cancer grows or spreads at any point while you are receiving study drugs, then you will stop the study drugs and your doctor will decide on another treatment for your cancer.

If your disease is stable, becomes smaller, or becomes undetectable, then you will continue receiving the study drugs for a total of 12 cycless, with 6 cycles given before surgery and 6 cycles given after surgery.

If you are not able to start the post-operative mFOLFIRINOX cycles within 12 weeks after your surgery, you will stop participating in the study, and your doctor will decide on another treatment for your cancer.

After the completion of the study drugs, you will take part in regular follow-up with your physician as follows:

For the first three years after completing mFOLFIRINOX, you will return to the clinic every 3 months. The following tests and procedures will be done every 3 months unless otherwise specified:

- A review of your medical history
- Aphysical examination including assessment of your weight and performance status
- 1-2 tablespoons of blood (or 15-30milliliters) will be collected for routine laboratory tests.
- An optional blood sample (10-20 milliliters) will be drawn for research purposes. You will be asked to indicate whether or not you agree to this sample at the end of this form. The choice to provide this sample is up to you. If you choose not to provide the sample, you can still participate in this study.
- You will also undergo a CT scan or MRI at six month intervals (within 4 weeks of your last dose of study drug(s) and then twice a year thereafter).

Four and five years after completing treatment, you will return to clinic every 6 months. The following tests and procedures will be done every 6 months unless otherwise specified:,

- A review of your medical history
- A physical examination including assessment of your weight and performance status
- 1-2 tablespoons of blood (or 15-30 milliliters) will be collected for routine laboratory tests.
- An optional blood sample (10-20 milliliters) will be drawn for research purposes. You will be asked to indicate whether or not you agree to this sample at the end of this form. The choice to provide this sample is up to you. If you choose not to provide the sample, you can still participate in this study.

- You will undergo a CT scan or MRI at 12 month intervals (once a year).

After five years, you will return to clinic annually or once a year until your cancer returns or death. The following tests and procedures will be done once a year:

- A review of your medical history
- A physical examination including assessment of your weight and performance status
- 1-2 tablespoons of blood (or 15-30 milliliters) will be collected for routine laboratory tests.
- An optional blood sample (10-20 milliliters) will be drawn for research purposes. You will be asked to indicate whether or not you agree to this sample at the end of this form. The choice to provide this sample is up to you. If you choose not to provide the sample, you can still participate in this study. You will also be asked to provide a sample when your disease progresses.
- You will undergo a CT scan or MRI at 12 month intervals (once a year).

You will be contacted annually by the team for survival follow-up information.

RISKS AND INCONVENIENCES

You may have side effects while on the study. You will be watched carefully by your doctor for any side effects while you are participating in this study. Side effects may be mild or very serious. You may experience side effects that were not expected or have not been reported previously; if new side effects are discovered, your doctor will know about them and share that information with you. Your health care team may give you treatments or reduce the doses of one or more of the chemotherapy drugs to help lessen side effects. Other drugs may be given to make the side effects less serious and less uncomfortable. Most side effects go away shortly after the chemotherapy is stopped. In some cases, side effects can be long-lasting. Although rare, in some cases side effects are permanent, serious, debilitating, or life-threatening. Death is a rare but possible result of serious side effects of chemotherapy.

Your doctor will check you closely to see if any of these side effects are occurring and routine blood tests will be done to monitor the effects of treatment. You should talk to your doctor about any side effects that you have while taking part in the study. Your doctor will tell you about side effects that should be reported immediately to your health care team, including but not limited to fever, diarrhea, altered mental status, and problems breathing after receiving your treatment.

Risks and side effects related to 5-fluorouracil:

More likely:

- Diarrhea
- Nausea which may be accompanied by vomiting
- Irritation of the mouth
- Decreased white blood cell count that increases your risk of infection
- Anemia
- Decreased number of platelets (that may cause easy bruising or bleeding)

- Nail changes
- Dry skin

Less likely:
- Sensitivity to the sun
- Irritation of the eyelids or eyes
- Increased tearing of the eyes and runny nose
- Dryness, redness, tingling, pain, cracking of skin of the palms and soles
- Rash
- Darkening of the skin, especially the palms and soles and nail beds
- Hair loss

Rare:
- Toxicity to the heart which can include chest pain, heart attack, or changes on an EKG
- Seizures
- Confusion
- Loss of balance

Risks and side effects related to Levoleucovorin:
Less likely:
- Nausea
- Vomiting
- Diarrhea
- Fatigue
- Allergic reaction which may include trouble breathing, itching, hives, changes in blood pressure, vomiting

Risks and side effects related to Oxaliplatin:
More likely:
- Sensitivity of the hands, feet, or mouth to cold temperatures
- Numbness or tingling that may involve the hands, feet or mouth
- Nausea which may be accompanied by vomiting
- Diarrhea
- Constipation
- Decreased white blood cell count which may increase your risk of infection
- Anemia which may cause you to feel tired
- Decreased number of platelets which may cause easy bruising or bleeding
- Fatigue (feeling tired or weak)
- Fever
- Headache
- Trouble sleeping

Less likely:

- Allergic reaction with redness of the face, itching, hives (red itchy rash)
- A sensation of tightening in the throat or airway
- Changes in blood tests that suggest irritation or inflammation of the liver
- Swelling

Rare:

- Toxicity to the lung causing cough and shortness of breath
- Sudden onset of anemia due to breakdown of red blood cells

Additional Information About the Risks of Oxaliplatin:
Exposure to cold: When receiving oxaliplatin, the nerves that affect your throat may be affected and cause a strange sensation when swallowing liquids or breathing cold air. You should avoid cold beverages while are you participating in this study. You may also notice a tingling and numbness or pain in your hands and feet that worsen on exposure to cold. Extra layers of clothing (gloves, mittens, and warm socks) may help these symptoms be less severe. Inflammation of the nerves can become worse during the time you are receiving treatment, and the risk of developing it increases with the amount of oxaliplatin you receive. This inflammation usually goes away after the treatment is stopped.

Very rarely, liver damage that can lead to chronic liver disease has been associated with oxaliplatin. Liver disease may appear as the enlargement of the liver and/or the spleen, abnormal blood flow to the liver, fluid retention in the abdomen and legs, and/or enlarged blood vessels in the esophagus that may cause internal bleeding.

Drugs similar to oxaliplatin have been known to cause leukemia in a small number of patients. It is not known whether the risk of future development of leukemia is a side effect of oxaliplatin.

Risks and side effects related to Irinotecan:
More likely:

- Diarrhea
- Nausea
- Vomiting
- Loss of appetite
- Decreased white blood cell count that increases your risk of infection
- Anemia
- Decreased number of platelets (that may cause easy bruising or bleeding)
- Hair loss
- Fatigue (feeling weak or tired)

Less likely:

- Constipation (trouble having bowel movements)
- Pain in the abdomen

- Runny nose and eyes
- Flushing (reddening of the face)
- Sweating
- Difficulty speaking, slurred speech, swollen tongue during or right after irinotecan*
- Stomach cramping and early diarrhea occurring during or right after the irinotecan*

*These early symptoms go away after the injection of the drug is stopped, and also may respond quickly to a medicine called atropine. If these immediate side effects occur, then you will get this medicine to prevent these symptoms with each following cycle

Rare:

- Skin rash
- Changes in certain blood tests that suggest irritation or inflammation of the liver
- Trouble sleeping
- Fever
- Shortness of breath
- For more information about risks and side effects, ask your study doctor.

BENEFITS

Taking part in this study may or may not have direct medical benefits for you. We cannot and do not guarantee that you will receive any benefits from this study. Possible benefits are shrinkage of your tumor, improvement in your symptoms related to your cancer, and prolonged survival. The information learned from the study may also help to benefit other patients with pancreatic cancer in the future.

ECONOMIC CONSIDERATIONS

You will not be paid for your participation in this study. You and/or your insurance payer will only be responsible for all charges related to or associated with chemotherapy and physician visits.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at:

http://cancer.gov/clinicaltrials/understanding/insurance-coverage

You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

TREATMENT ALTERNATIVES

There are other alternatives besides participation in this study, which could be considered for you. These alternatives include, but are not limited to:

(1) treating your cancer with initial surgery followed by chemotherapy
(2) treating your cancer with different drugs or combinations of drugs followed by surgery
(3) treating your cancer with radiation followed by surgery
(4) taking part in another clinical trial.

Alternatively, you can choose to receive no anti-cancer treatments at all, but only care to make you feel more comfortable. Talk to your doctor about your choices before you decide if you will take part in this study.

Should your disease become worse, or the side effects become very severe, or new scientific developments occur, or your study doctor feels that this treatment is no longer in your best interest, the study drugs will be stopped. Your study doctor can provide detailed information regarding your cancer and the benefits of other treatment options.

CONFIDENTIALITY AND PRIVACY

Any identifiable information that is obtained in connection with this study will remain confidential and will be disclosed only with your permission or as required by U.S. or State law. Examples of information that we are legally required to disclose include abuse of a child or elderly person, or certain reportable diseases. When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity unless your specific consent for this activity is obtained.

We understand that information about you obtained in connection with your health is personal, and we are committed to protecting the privacy of that information. If you decide to be in this study, the researcher will get information that identifies you and your personal health information. This may include information that might directly identify you, such as your name, date of birth, and information about your disease. This information will be de-identified at the earliest reasonable time after we receive it, meaning we will replace your identifying information with a code that does not directly identify you. The principal investigator will keep a link that identifies you to your coded information, and this link will be kept secure and available only to the PI or selected members of the research team. Any information that can identify you will remain confidential.

The research team will only give this coded information to others to carry out this research study. The link to your personal information will be kept until all study procedures and data collection analysis is completed, after which time the link will be destroyed and the data will become anonymous. The data will be kept in this anonymous form indefinitely.

Information about your study participation will be entered into your Electronic Medical Record (EMR). Once placed in your EMR, these results are accessible to all of your providers who

participate in the EMR system. Information within your EMR may also be shared with others who are appropriate to have access to your EMR (e.g., health insurance company, disability provider.)

The information about your health that will be collected in this study includes:

- Records about phone calls made as part of this research
- Records about your study visits
- Physical exams
- Laboratory, x-ray, and other test results
- Records about the study drug you received

Information about you and your health which might identify you may be used by or given to:

- The U.S. Department of Health and Human Services (DHHS) agencies and other federal research oversight agencies
- Representatives from Yale University and the Human Investigation Committee (the committee that reviews, approves, and monitors research on human subjects), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.
- Your providers who are participants in the Electronic Medical Record (EMR) system
- Yale Cancer Center's Protocol Review Committee and the staff of the Yale Cancer Center Clinical Trials Office who are directly involved in the study.
- Those individuals at Yale who are responsible for the financial oversight of research including billings and payments
- The Principal Investigator, Jill Lacy, MD, and the Yale study team
- The U.S. Food and Drug Administration (FDA) This is done so that the FDA can review information about the chemotherapy regimen involved in this research.
- Health care providers who provide services to you in connection with this study
- Laboratories and other individuals and organizations that analyze your health information in connection with this study, according to the study plan.
- Co-Investigators and other investigators
- Study Coordinator and Members of the Research Team
- Data and Safety Monitoring Board and others authorized to monitor the conduct of the Study

A description of this clinical trial will be located on http: www.ClinicalTrials.gov, as required by United States Law (U.S. Federal Food, Drug and Cosmetic Act ("FD&C") and Public Health Service ("PHS") Act). 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 anytime.

By signing this form, you authorize the use and/or disclosure of the information described above for this research study. The purpose for the uses and disclosures you are authorizing is to ensure

that the information relating to this research is available to all parties who may need it for research purposes.

All health care providers subject to HIPAA (Health Insurance Portability and Accountability Act) are required to protect the privacy of your information. The research staff at the Yale School of Medicine and Yale New Haven Hospital is required to comply with HIPAA and to ensure the confidentiality of your information. Some of the individuals or agencies listed above may not be subject to HIPAA and therefore may not be required to provide the same type of confidentiality protection. They could use or disclose your information in ways not mentioned in this form. However to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

If you decide to participate in this study, you will be asked to authorize these uses and disclosures by signing this form. You must authorize these uses to participate in this study. This authorization to use and disclose your health information collected during your participation will never expire.

You may change your mind and decide to withdraw your permission for the sponsor to use health information from your medical records at any time by telling the study staff or by sending a written request to Jill Lacy, MD, Yale Cancer Center, 333 Cedar St. FMP 116, New Haven, CT, 06520. If you withdraw your permission, your participation in the study will end. However, this withdrawal will not affect your future treatment or medical management in any way, and you will not lose any benefits to which you are otherwise entitled.

Your privacy and confidentiality of the study records will be protected to the fullest extent provided by law. Research staff on this study will have access to research related information contained in your study record.

Your experience, while on this trial, will be recorded in Yale-sponsored case report forms. Your name will not be recorded on these case report forms; instead a study number will be used. In addition, a copy of your medical record will be stored at the Yale Cancer Center Clinical Trials Office (CTO). The CTO is locked and accessible only to staff members of that office. Access to the hospital information is limited to clinical staff treating you at the Yale Cancer Center Oncology Clinic and research staff involved in this study.

IN CASE OF INJURY

If you are injured as a result of your participation in this study, you need to contact the study doctor Jill Lacy, M.D., 203-737-1600 as soon as you are able, to receive the provided treatment. You or your insurance carrier will be expected to pay the costs of this treatment. No additional financial compensation for injury or lost wages is available.

You do not give up any legal rights by signing this form.

WHERE TO GET MORE INFORMATION

You may call the National Cancer Institute's Cancer Information Service at:
1-800-4-CANCER (1-800-422-6237) or TTY: 1-800-332-8615

You may also visit the NCI Web site at http://cancer.gov/

For NCI's clinical trials information, go to: http://cancer.gov/clinicaltrials/

For NCI's general information about cancer, go to http://cancer.gov/cancerinfo/

VOLUNTARY PARTICIPATION AND WITHDRAWAL

Participation in this study is voluntary. You are free to choose not to participate in this research study. Refusing to take part in this research study will not lead to penalty or loss of benefits to which you are otherwise entitled (such as your health care outside the study, the payment for your health care, and your health care benefits). However, you will not be able to enroll in this research study and will not receive study procedures as a study participant if you do not allow use of your information as part of this study.

Withdrawing from the Study:

If you decide to participate in this research study, you are free to stop and withdraw from this study at any time during its course. To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part. They will make sure that proper procedures are followed and a final visit is made for your safety. This will cancel any future research study appointments.

The researchers may withdraw you from participating in the research if necessary.

Withdrawing from the study will involve no penalty or loss of benefits to which you are otherwise entitled. It will not harm your relationship with your own doctors or with Yale-New Haven Hospital.

If you fail to give your consent by not signing this document, or if you cancel your consent later, then you will not be eligible to participate in this study and will not receive any treatment provided as part of the study. Unless and until you do cancel the consent, it will remain valid and effective.

Withdrawing Your Authorization to Use and Disclose Your Health Information:

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by telling the study staff or by sending written notice to the study doctor, Dr. Jill Lacy, at the address listed on page one of this form. If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given

to others until the end of the research study, as necessary to insure the integrity of the study and/or study oversight

QUESTIONS

We have used some technical terms in this form. Please feel free to ask about anything you don't understand and to consider this research and the consent form carefully – as long as you feel is necessary – before you make a decision.

OPTIONAL TUMOR TISSUE AND BLOOD SAMPLES FOR RESEARCH PURPOSES

You are invited to provide access to samples (specimens) of your tumor tissue from a previous biopsy and provide blood samples and related information to be stored (banked) in a research tissue and specimen bank where it can be used for future research projects. The tumor tissue and blood specimens collected in this bank will be used by your treating physicians and collaborating researchers in the Yale Cancer Center to study biomarkers that predict the biology, pathology, and treatment of pancreatic cancer. This may help researchers in the future learn more about how to prevent, diagnose, and treat pancreatic cancer.

Study Procedures

If you decide to donate samples of your blood, a sample of blood will be collected from you at screening (30 milliliters), within 4 weeks of your surgery (10-20 milliliters), within 12 weeks of after your surgery on Cycle 7 Day 1 (10-20 milliliters), during post-treatment follow-up (10-20 milliliters) every 3 months for 3 years, every 6 months for two years, then annually until disease progression, and at the time of disease progression.

If you decide to provide access to samples of your tumor tissue from a previous biopsy (or archival tumor tissue), the researchers will analyze the previously collected tissue at any point during your participation on study. A new biopsy of your tumor is not required because previously collected tissue will be used.

How Your Tumor Tissue and Blood Specimen Gets Into the Databank

The archival tumor tissue and blood specimens that you donate for this research study will be sent to the Yale research tissue and blood specimen bank designated for this study along with the following information about you which will be entered into a computer (the database) that is used for research purposes.

The following information about you will be entered into the database: name, medical record number, date of birth, sex, information from medical history and physical examination, dates of tissue and blood specimen collection, results of laboratory tests, x-ray studies, imaging studies; the treatments you received and your response to treatments.

How Your Tumor Tissue and Blood Specimen Is Stored and Used for Future Research

The researchers who are responsible for entering and protecting your information in the database will use your information to study the biology, pathology, and treatment of pancreatic cancer.

When your specimens and information are stored, we are careful to try to protect your identity from discovery by others. Strict security safeguards are in place to reduce the chance of misuse or unplanned release of information.

Whenever possible, the researchers will use your information in a de-identified manner. De-identified means that the researchers will remove your name or any other personal identifier, such as medical record number, from your sample and label the sample with a unique code before analyzing the sample(s). In some cases they may use some identifying information about you for research purposes, subject to an approval process undertaken by the Yale Human Investigation Committee (HIC). (The HIC is an ethics committee that reviews, approves and monitors research on human subjects.) At times the researchers will use your information with a code, instead of your name; the code would allow results of the research to be linked back to you.

Your specimens will be stored for an unlimited time, and may be used to make a cell line that will live indefinitely. Future research may look at your genes, which are the units of inheritance that are passed down from generation to generation. Genes are responsible for many things about you such as eye color, hair color, blood type and hundreds of other traits. Future genetic analysis may possibly include finding out the details of how your DNA is put together, such as whole exome or genome sequencing, or genome wide association studies(that is, looking at genes other than those associated with a specific disease). The materials at some point may be injected into animals in some of the research. We expect that there will be widespread sharing of these specimens and associated information.

There is a risk that your information could be misused. The chance of this happening is very small. We have protections in place to lower this risk. There can also be a risk in uncovering genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a research study. Very rarely, health or genetic information could be misused by employers, health insurance companies, and others. There is a federal law called the Genetic Information Nondiscrimination Act (GINA) that, in general, makes it illegal for health insurance companies, group health plans, and most employers, except those with fewer than 15 employees, to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Risks and Inconveniences

There are no physical risks to you for donating and storing your archival tumor tissue and blood samples for use in future research studies. You will not be required to give any more tumor tissue or to undergo any additional procedures than that which will be necessary for clinical purposes. You will be required to give an additional sample of blood (up to two tablespoons, or 15-30 milliliters) as explained above. These additional samples of blood will be taken at the same time as other blood tests are being drawn as a part of your clinical care, and you will not be required to have a separate blood draw procedure to obtain these blood samples. In the unlikely chance that your information is viewed by someone outside the research team however, there is a risk of breach of confidentiality.

Benefits

Using your specimens for research will probably not help you. We do hope the research results will help people in the future. We hope that the information we learn in future research studies will increase our knowledge of human health and that this information will lead to better prevention, diagnoses and treatments in the future.

Economic Considerations

You will not receive any payments for donating your archival tumor tissue, blood samples or related information into the research data bank.

Your specimens and information will only be used for research and will not be sold. There is a possibility that this research may lead to development of products that will be commercialized. If this happens, there is no plan to share any financial gain with you.

Voluntary Participation and Withdrawal

You are free to choose not to donate your archival tumor tissue, blood specimens and related information to research. If you agree to provide the specimens and related information, you are free to change your mind at any time, but the researchers may still use the information collected before you changed your mind in order to complete the research that has already started. The researchers will anonymize the tissue

and blood specimens and related information by removing and destroying all identifiers and links to identifiers so that it cannot be associated with you, but the researchers will not destroy the tissue and blood specimens and related information.

If you choose not to allow your information/samples to be stored and used, or if you withdraw your permission, this will not harm your relationship with the study doctors, with Yale University or Yale-New Haven Hospital. To withdraw from the optional sample study, you tell the study staff or send written notice to the study doctor, Dr. Jill Lacy, at the address listed on page one of this form.

OPTIONAL BLOOD SAMPLES FOR RESEARCH PURPOSES (check one):

☐ Yes, I agree to donate my blood samples and related information as explained above for research purposes.

☐ No, I do not agree to donate my blood samples and related information as explained above for research purposes.

OPTIONAL BLOOD SAMPLES FOR RESEARCH PURPOSES (check one):

☐ Yes, I agree to donate my archival tumor tissue and related information as explained above for research purposes.

☐ No, I do not agree to donate my archival tumor tissue and related information as explained above for research purposes.

Authorization and Permission

I have read (or someone has read to me) this form and have decided to participate in the project as described above. Its general purposes, the particulars of my involvement and possible hazards and inconveniences have been explained to my satisfaction. My signature also indicates that I have received a copy of this consent form.

By signing this form, I give permission to the researchers to use and give out information about me for the purposes described in this form. By refusing to give permission, I understand that I will not be able to participate in this research.

I also confirm that I have received a Trial Alert Card providing contact details of the study doctor and agree to carry this card with me at all times.

Study Participant (print name)	Signature	Date
Person obtaining consent (print name)	Signature	Date
Person obtaining consent (print name) – only if applicable, otherwise blank	Signature	Date
Interpreter/ Witness (print name) – only if applicable, otherwise blank	Signature	Date

If after you have signed this form you have any questions about your privacy rights, please contact the Yale Privacy Officer at (203) 432-5919.

If you have further questions about this project or if you have a research-related problem, you may contact the Principal Investigator, Dr. Jill Lacy at 203-737-1600. If you would like to talk with someone other than the researchers to discuss problems, concerns, and questions you may have concerning this research, or to discuss your rights as a research subject, you may contact the Yale Human Investigation Committee at (203) 785-4688.