UNIVERSITY OF PENNSYLVANIA
RESEARCH SUBJECT
INFORMED CONSENT AND HIPPA AUTHORIZATION FORM

Protocol Title: A Randomized Phase II/Genomic Trial of two chemotherapy regimens in patients with resected pancreatic adenocarcinoma

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Emergency Contact: 24 Hour Emergency – Call 215-662-6059
Ask for Oncologist On-Call

Why am I being asked to volunteer?

You are being invited to participate in a research study. Your participation is voluntary which means you can choose whether or not you want to participate. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. The research team is going to talk to you about the research study, and they will give you this consent form to read. You may also decide to discuss it with your family, friends, or family doctor. You may find some of the medical language difficult to understand. Please ask the study doctor and/or the research team about this form. If you decide to participate, you will be asked to sign this form.

IRB Approved from: 03/10/2016 to: 01/07/2017

BACKGROUND

You have been diagnosed with pancreatic cancer. Treatment for pancreatic cancer involves surgery as well as chemotherapy (usually with a drug called Gemzar or gemcitabine), radiation therapy, or a combination of both (chemoradiotherapy) used after surgery (adjuvant therapy. For patients like you with pancreatic cancer for whom surgery is an option, routine care is surgery followed by chemoradiation therapy.

Doctors at the University of Pennsylvania, Abramson Cancer Center, are conducting a study looking at comparing two chemotherapy regimens given before and after chemoradiation. All of the drugs used in this study are approved by the US Food and Drug Administration (FDA) for the treatment of cancer. Both treatment regimens used in this study have been previously studied and shown to improve survival when comparerd to gemcitabine alone. The first regimen is called FOLFIRINOX. This is a regimen which includes 5-flourouracil, leucovorin, irinotecan and oxapliplatin. The other regimen being studied is gemcitabine and abraxane.

What is the purpose of this research study?

The overall goal of this clinical trial is to learn which of these treatment regimens is more effective at reducing the risk of your pancreatic cancer recurring after surgery. This study also intends to look at blood and tissue samples to help doctors better understand who is at risk for cancer recurrence. All patients will receive standard treatment for their disease: surgery followed by chemoradiation.

How long will I be in the study? How many other people will be in the study?

It is estimated that patients enrolled in this study will participate for about 6 months while on treatment. After you complete treatment, we will check on how you are doing by calling you or reviewing your medical record chart for the rest of your life. The study plans to enroll up to 50 patients with pancreatic cancer for whom surgery and chemoradiation is the recommended treatment plan.

What am I being asked to do?

Before you begin the study:
You will need to have the following exams, tests or procedures to find out if you can be in the study. These exams, tests and procedures are part of routine cancer care, and may be done even if you do not join the study. These visits will occur in the outpatient clinic and will take approximately 30-60 minutes. If you have had some of these tests recently, they may not need to be repeated. This will be up to your study doctor and this will be discussed with you. These assessments must be done within 4 weeks of starting this study.

These tests/procedures will be performed during the screening visit.

- Review of your medical history including any medications that you may have taken recently or are currently taking, other medical problems you may have, and other treatments you have received for your cancer and how you responded to them.
- Complete physical examination - including review of height/weight, blood pressure and heart rate and an assessment of your ability to perform daily life activities (i.e. walking, house work, etc).
- Routine blood tests - about 2 tablespoons of blood will be drawn to check for the following:
  - Blood cell counts (number of each type of blood cell)
  - Blood chemistry levels (to test your kidney and liver function and the minerals in your blood)
  - Tumor markers (CA19.9): Tumor markers are molecules occurring in blood or tissue that are associated with cancer and whose measurement or identification is useful in patient diagnosis or clinical management
  - Collection of one tube of blood, for research purposes only, to test for elements that might help predict who is at risk of disease recurrence
- Pregnancy test - if you are a woman of child-bearing potential. A sample of your blood or urine will be needed to complete this test. This test must be done within 72 hours of starting the study drug. If you are pregnant, you cannot participate in this study.
- Radiology tests – routinely used to assess your disease. These assessments may include a CT (computed tomography) scan, MRI (magnetic resonance imaging) scan, PET/CT (positron emission tomography/computed tomography) scan. These are routine procedures used to help doctors monitor your cancer. Your study doctor will explain these tests to you in more detail and let you know which type of scan(s) you will receive. The same type of scans will be used throughout your participation on this study as these scans are standard of care for your disease.

It is possible that after these tests are reviewed, you will not be able to take part in this study. There may be other reasons why you cannot participate. Your study doctor will discuss these with you. It is important that you answer all of the questions asked by the study staff honestly and completely.

Study Treatment

When all of the above tests have been completed, and if you have been found to be eligible to enter this study, and you agree to participate, you will be scheduled to return to the clinic to begin treatment on this study. Which treatment you receive will be determined by a process called randomization. This means that you will be randomly (by chance) assigned to receive either FOLFIRINOX or gemcitabine/abraxane. You will be informed of which treatment arm to which you are assigned. If there are challenges with your insurance company, you will be offered the alternative treatment arm. If your insurance company fails to cover the cost of drugs on either arm, you will not be able to participate in this study.

If you are randomized to receive FOLFIRINOX, treatment is as follows beginning on Day 1 of each 2-week treatment cycles for a total of 4 cycles or 8 weeks:

Oxaliplatin – 2 hour intravenous (IV, into a vein) infusion

Irinotecan – 90 minute IV infusion

Leucovorin – 2 hour IV infusion

5Fluorouracil (5FU) – given 2 ways

- As a quick (bolus) IV injection given by a nurse in the infusion suite through the IV tubing with a 5FU-filled syringe, followed by
- An outpatient, 46 hour continuous IV infusion provided by a home IV infusion company. The 5FU is delivered by a small pump worn in a fanny pack around the waist. The home IV infusion company will arrange your disconnect at the end of the infusion. If you do not already have one, you will need a "port" or pique line inserted into a vein.

On Day 1 of each treatment cycle, you will be in the infusion suite for about 6 hours for treatment. All drugs will be administered at standard doses and adjusted downward should you experience unacceptable or intolerable side effects.

Following 8 weeks of FOLFIRINOX, you will wait at least 28 days, and then you will be referred to Radiation Oncology to receive chemoradiation as is standard of care for your disease. Doctors in Radiation Oncology will review the processes and procedures for chemoradiation as well as the risks, and you will be asked to sign the University of Pennsylvania's consent for chemoradiation therapy. Briefly, chemoradiation requires that you have a "port" or some form of IV access that allows for the continuous infusion of a drug called 5-FU that is used to make radiation therapy even more effective. Radiation therapy will take 5 ½ weeks to complete. You will receive radiation therapy 5 days per week for 5½ weeks. During the time you are receiving radiation treatment you

will also be receiving chemotherapy daily by continuous infusion, (7 days per week) with the medication 5-FU (Fluorouracil).

After completed chemoradiation, you will repeat the 8 weeks of chemotherapy with FOLFIRINOX, as described above.

If you are randomized to receive gemcitabine/abraxane, treatment is as follows beginning on Day 1 of each 4-week treatment cycle for a total of 2 cycles or 8 weeks:

Gemcitabine – 30 minute intravenous (IV, into a vein) infusion, repeated days 8 and 15

Abraxane – 30 minute intravenous (IV, into a vein) infusion, repeated on days 8 and 15

On Days 1, 8 and 15 of each treatment cycle, you will be in the infusion suite for about 2-3 hours for treatment. All drugs will be administered at standard doses and adjusted downward should you experience unacceptable or intolerable side effects.

Following 8 weeks of gemcitabine/abraxane, you will wait at least 28 days, and then you will be referred to Radiation Oncology to receive chemoradiation as is standard of care for your disease. Doctors in Radiation Oncology will review the processes and procedures for chemoradiation as well as the risks, and you will be asked to sign the University of Pennsylvania's consent for chemoradiation therapy. Briefly, chemoradiation requires that you have a "port" or some form of IV access that allows for the continuous infusion of a drug called 5-FU that is used to make radiation therapy even more effective. Radiation therapy will take 5 ½ weeks to complete. You will receive radiation therapy 5 days per week for 5½ weeks. During the time you are receiving radiation treatment you will also be receiving chemotherapy daily by continuous infusion, (7 days per week) with the medication 5-FU (Fluorouracil).

After completed chemoradiation, you will repeat the 8 weeks of chemotherapy with gemcitabine/abraxane, as described above.

Tests/Procedures:

You will be asked to come into the clinic for tests/procedures during the course of this study. These exams, tests or procedures are part of routine cancer care for patients with pancreatic cancer. In general, you will have a physical exam on day 1 of each treatment cycle, routine blood work every 1-2 weeks and scans to assess your disease at end of treatment and then every 4-6 months as part of routine follow up.

At each of these study visits you will be asked how you are feeling, if you have had any side effects, and about any medications you are taking. You must tell your study doctor about all the medications you are taking throughout your participation in this research study since the effects of this study drug taken with other medications are not known.

What are the possible risks or discomforts?

While on the study, you are at risk for the following side effects. Some of these side effects may be potentially serious or life-threatening, and may include death. You should discuss these with the study doctor. There may be side effects that are currently not known to us. If you experience side effects from this treatment, your study doctor may delay or skip a dose of the study drug, reduce the doses or ask you to stop study treatment. Your doctors may also give you drugs to help lessen these side effects. Many side effects go away shortly after the treatment is stopped, but in some cases side effects can be serious, long lasting or permanent. You should talk to your study doctor about any side effects that you have while taking part in this study.

Risks associated with 5-FU:

The following side effects are common (occurring in greater than 30%) for patients taking 5-FU:

- Diarrhea.
- Nausea and possible occasional vomiting.
- Mouth sores.
- Poor appetite.
- Watery eyes, sensitivity to light (photophobia).
- Taste changes, metallic taste in mouth during infusion.
- Discoloration along vein through which the medication is given.
- Low blood counts. Your white and red blood cells and platelets may temporarily decrease. This can put you at increased risk for infection, anemia and/or bleeding.

Nadir: Meaning low point, nadir is the point in time between chemotherapy cycles in which you experience low blood counts.

Onset: 7-10 days
Nadir: 9-14 days
Recovery: 21-28 days

These side effects are less common side effects (occurring in about 10-29%) of patients receiving 5-FU:

- Skin reactions: Dry, cracking, peeling skin. Darkening of the skin (hyperpigmentation), darkening of the skin where previous radiation treatment has been given (radiation recall).
- Hair thinning.
- Nail changes - discoloration, loss of nails (rare).

- Hand -foot syndrome (Palmar-plantar erythrodysesthesia or PPE) -skin rash, swelling, redness, pain and/or peeling of the skin on the palms of hands and soles of feet. Usually mild, starting 5-6 weeks after start of treatment. May require reductions in the dose of the medication.

Serious adverse reactions to 5-FU are; chest pain, EKG changes and increases in cardiac enzymes - which may indicate problems with the heart. These symptoms are very rare but increased for patients with a prior history of heart disease.

The use of oxaliplatin in combination with 5-FU has, in very rare cases, been associated with a risk of veno-occlusive disease (VOD) of the liver, a form of serious liver injury. Signs of VOD include enlarged liver, fluid accumulation in the abdomen and jaundice (yellowing of the skin and eyes). VOD can result in permanent liver damage, enlarged spleen, serious systemic hypertension (high blood pressure) and a twisting of the veins in the esophagus (can cause bleeding, nausea, vomiting and may require surgical repair).

Risks associated with Leucovorin (LV): Leucovorin is generally well tolerated with rare allergic reactions being the most common side effect. LV can also cause nausea, diarrhea and mouth sores. In rare cases, it may cause seizures or low blood calcium levels.

Risks associated with Oxaliplatin:

Oxaliplatin Infusion Related Side Effects:

- The feeling of difficulty swallowing, shortness of breath, jaw spasm, abnormal tongue sensation and feeling of chest pressure. This has been reported rarely (<5%). It generally starts within hours of Oxaliplatin infusion and often occurs upon exposure to cold. Avoiding exposure to cold helps to prevent this adverse reaction. Future Oxaliplatin infusions may be given over a longer time frame to help reduce the incidence.

The following Oxaliplatin side effects are common (occurring in greater than 30%) for patients taking Oxaliplatin:

- Peripheral neuropathy - Numbness and tingling and cramping of the hands or feet often triggered by cold. This symptom will generally lessen or go away between treatments, however as the number of treatments increase the numbness and tingling will take longer to lessen or go away. Your health care professional will monitor this symptom with you and adjust your dose accordingly.
- Nausea and vomiting
- Diarrhea
- Mouth sores

- Low blood counts - Your white and red blood cells and platelets may temporarily decrease. This can put you at increased risk for infection, anemia and/or bleeding.
- Fatigue
- Loss of appetite
- Shortness of breath
- Lung disease
- Kidney problems
- Visual/hearing loss

The following are less common Oxaliplatin side effects (occurring in 10-29%) for patients receiving Oxaliplatin:

- Constipation
- Fever
- Generalized pain
- Headache
- Cough
- Temporary increases in blood tests measuring liver function.
- Allergic reaction: a rare side effect, however, call for help immediately if you suddenly have difficulty breathing, your throat feels like it is closing, or chest pain. Other signs of allergic reaction include rash, hives, sudden cough, or swelling of the lips or tongue.

Risks associated with irinotecan:

The following side effects are common (occurring in greater than 30%) for patients taking Irinotecan:

- Diarrhea; two types early and late forms.
- Early diarrhea: Occurring within 24 hours of receiving drug, accompanied by symptoms runny nose, increased salivation, watery eyes, sweating, flushing, abdominal cramping. (This can occur while the drug is being administered. If so, alert your healthcare professional promptly. Medication can be given to stop and/or lessen this early side effect).
- Late diarrhea: Occurring greater than 24 hours of receiving drug, usually peaks at about 11 days after treatment. Because of concerns of dehydration and electrolyte imbalances with diarrhea it is important to be in contact with health care professionals for monitoring, and for medication and diet modifications advice.
- Nausea and vomiting.
- Weakness.
- Low white blood cell count. (This can put you at increased risk for infection).
- Low red blood cell count (anemia).

Nadir: Meaning low point, nadir is the point in time between chemotherapy cycles in which you experience low blood counts.

Onset: 10 days
Nadir: 14-16 days
Recovery: 21-28 days

- Hair loss
- Poor appetite
- Fever
- Weight loss

These side effects are less common side effects (occurring in about 10-29%) of patients receiving Irinotecan:

- Constipation
- Shortness of breath
- Insomnia (see sleep problems)
- Cough
- Headache
- Dehydration
- Chills (see flu-like symptoms)
- Skin rash (see skin reaction)
- Flatulence (see abdominal pain)
- Flushing of face during infusion
- Mouth sores
- Heartburn
- Swelling of feet and ankles

Risks associated with Gemcitabine (also known as Gemzar):

The following side effects are common (occurring in more than 30%) for patients taking Gemcitabine:

- Flu-like symptoms(muscle pain, fever, headache, chills, fatigue)
- Fever (within 6-12 hours of first dose)
- Fatigue
- Nausea (mild)
- Vomiting
- Poor appetite
- Skin rash
- Low blood counts. Your white and red blood cells and platelets may temporarily decrease. This can put you at increased risk for infection, anemia and/or bleeding.

Nadir: Meaning low point, nadir is the point in time between chemotherapy cycles in which you experience low blood counts.

Onset: none noted
Nadir: 10-14 days
Recovery: day 21

- Temporary increases in liver enzymes
- Blood or protein in the urine

These are less common side effects (occurring in 10-29%) for patients receiving Gemcitabine:

- Diarrhea
- Weakness
- Hair loss
- Mouth sores
- Difficulty sleeping
- Shortness of breath
- Hearing disorders

Risks associated with Abraxane:

The following side effects are common (occurring in greater than 30%) for patients taking Abraxane:

- Low blood counts (your white and red blood cells may temporarily decrease which can put you at increased risk for infection and/or anemia)
- Hair loss
- Nausea
- Abnormal ECG (electrocardiogram)
- Peripheral neuropathy (numbness and tingling of hands and feet)
- Arthralgias and myalgias, pain in the joints and muscles (usually temporary occurring 2-3 days after Abraxane, and resolve within a few days)
- Weakness and fatigue
- Increases in blood tests measuring liver function (these return to normal once treatment is discontinued)

The following are less common side effects for patients receiving Abraxane:

- Infections
- Diarrhea
- Vomiting
- Mouth sores
- Swelling of feet or ankles
- Shortness of breath
- Eye problems

This lists above include common and less common side effects for patients taking these drugs. Side effects that are very rare -- occurring in less than about 10 percent of patients -- are not listed here. But you should always inform your health care provider if you experience any unusual symptoms.

Risks from the medications used along with chemotherapy

- Before chemotherapy, you may receive dexamethasone (Decadron®) to help with any nausea you may experience. Dexamethasone may have any or none of the following side effects: increased blood sugars, elevation of blood pressure, increase in white blood cell count, difficulty sleeping, mania, hallucinations (seeing, hearing, feeling, or smelling things that do not exist), unreal thoughts and difficulty with reality.
- You may receive loperamide to help prevent or treat diarrhea you may get from some of these chemotherapies. Loperamide may have any or none of the following side effects: fatigue, nausea, dizziness, vomiting, rash, difficulty emptying the bladder, headache, irritability, increased blood sugar, increase urine production. You may have received these medicines even if you were not enrolled in this study if you decided to receive chemotherapy.

Risks of Chemoradiation

The risks of chemoradiation will be discussed with you when you meet with the radiation oncologist but they include:

Risks of Radiation

- nausea
- stomach pain and intestinal discomfort (generally goes away 2 months after treatment is finished)
- loss of appetite
- weight loss
- mild muscle aches in the area treated
- hair loss
- fatigue
- low blood counts
- skin rash
- skin redness
- inflammation of the mucous membranes, that is, painful sores in the mouth

Rare but serious side effects related to the radiation include

- change in liver or kidney function, which is unlikely to cause symptoms

- bowel obstruction, resulting in abdominal pain, nausea and vomiting and may require surgery.

- **Risk of the chemotherapy (5-FU) during the chemoradiation** treatment

(Occurring in >30% of patients)
- diarrhea
- mouth sores
- poor appetite
- nausea
- possibly vomiting
- fatigue
- taste changes
- low blood counts
- watery eyes
- eye sensitivity to light (photophobia)

These side effects are less common (occurring in about 10-29%) of patients receiving 5-FU:
- skin reactions such as dryness, cracking, peeling skin or darkening of the skin
- hair thinning
- nail changes
- hand-foot syndrome – swelling, redness, pain and/or peeling of the skin on the palms of hands and soles of feet

A separate consent form will be used and required for chemoradiation therapy.

Risks of Blood Drawing

Routine needle sticks for blood samples or starting IVs may cause pain, bruising, or infection at the site where the needle enters your body. It is also possible that you may feel lightheaded or faint.

Reproductive Risks

You should not become pregnant or father a child while on this study and for at least 90 days after your last dose of study treatment, because it is not known if these drugs have an effect on an unborn baby. In addition, women should not breastfeed while on this study as these drugs may also affect a breast-feeding child. Pregnant women and women who are breast-feeding are not allowed to participate in this study.

Female Participants

If you are a woman who is able to become pregnant, you will be asked to have a pregnancy test at the beginning of the study to determine if you are pregnant. If you are

pregnant, you will not be able to participate in this study. You should not become pregnant while on this study, or for 90 days after receiving your last dose of study treatment.

If you are able to become pregnant, you must agree to use a medically accepted form of birth control during the course of this study and for at least 90 days after your final study treatment. Medically accepted forms of birth control include condoms, diaphragm, cervical cap, the placement of an intrauterine device (IUD), birth control pills, hormone implants or injections, OR a partner who has undergone a vasectomy (surgical sterility), OR you must agree to completely abstain from intercourse for two weeks before you begin study treatment, during participation in this study, and for 90 days after your final study treatment. Abstinence at certain times of the cycle only, such as during the days of ovulation or after ovulation, and withdrawal are not acceptable methods of birth control. Your study doctor must approve your form of birth control. Ask your study doctor about the contraceptive methods that are available and which might be the best for you.

Even when you use an approved contraceptive method, there is always a small risk that you could still become pregnant. If you do become pregnant during the course of this study, you must discontinue study treatment, tell the investigator immediately, and consult an obstetrician or maternal-fetal specialist. The study doctor will also ask to follow-up on the pregnancy and the condition of your newborn.

Men

The effect of the investigational drugs on the male reproductive system (sperm) is unknown; therefore you should not father a child while participating in this study and for at least 90 days after your final study treatment. If your spouse or partner has the potential to become pregnant, you and your spouse/partner must agree to use a medically accepted form of birth control during the course of this study and for at least 90 days after your final study treatment. If your partner does become pregnant, you must inform your study doctor immediately

Medically accepted forms of birth control methods include condoms, diaphragm, cervical cap, the placement of an intrauterine device (IUD), birth control pills, hormone implants or injections, or surgical sterility (vasectomy). OR you must agree to completely abstain from intercourse for two weeks before you begin study treatment, during participation in this study, and for 90 days after your final study treatment. Abstinence at certain times of the month only, such as during the days of ovulation or after ovulation, or withdrawal are not acceptable methods of birth control. Your study doctor must approve your form of birth control. Ask your study doctor about the contraceptive methods that are available and which might be the best for you.

You should also inform your partner of the potential harm to an unborn child. She should know that if a pregnancy should occur, you will need to report it to the study doctor immediately, and she should promptly notify her doctor and consult an

obstetrician or maternal-fetal specialist. The study doctor will also ask to follow-up on the pregnancy and the condition of your newborn. For more information about risks and side effects, please ask your study doctor.

What if new information becomes available about the study?
During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available. A description of this clinical trial will be available on http://www,clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of results. You can search this website at any time.

What are the possible benefits of the study?

Although benefit cannot be guaranteed, it is possible that your risk for recurrence of pancreatic cancer will be lessened. Also, what is learned from this study may benefit pancreatic cancer patients in the future.

What other choices do I have if I do not participate?

Participating in this study is completely voluntary. If you do not participate, you can still have chemoradiation, just chemotherapy or just radiotherapy.

Will I be paid for being in this study?

No, you will not be paid for participating in this clinical trial.

Will I have to pay for anything?

Blood samples that were identified as research samples will be paid for by the study. All other tests, procedures, visits and treatments are considered standard of care for your disease. You and/or your health insurance will be billed for the costs of medical care during this study if these expenses would have happened even if you were not in the study, or if your insurance agrees in advance to pay. These include routine office visits, surgery, routine blood tests, gemcitabine, chemoradiation and scans to assess your disease. All co-pays and deductibles will still apply. Please talk to your doctor and study team about putting you in touch with a financial counselor to determine exactly what the deductible and co-pay will be for you; this is highly variable depending on type on insurance.

What happens if I am injured from being in the study?

If you have a medical emergency during the study you should go to the nearest emergency room. You may contact the Principal Investigator or Emergency contact listed on page one of this form. You may also contact your own doctor, or seek

treatment outside of the University of Pennsylvania. Be sure to tell the doctor or his/her staff that you are in a research study being conducted at the University of Pennsylvania. Ask them to call the telephone numbers on the first page of this consent form for further instructions or information about your care.

We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

There are no plans for the University of Pennsylvania to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

If you think you have been injured as a result of taking part in this research study, tell the person in charge of the research study as soon as possible. The researcher's name and phone number are listed in the consent form.

When is the Study over? Can I leave the Study before it ends?

Each subject's participation is expected to last for 6 months. Your participation is entirely voluntary and you are free to leave the study at any time without compromising your ongoing or future care.

This study is expected to end after all participants have completed all visits, and all information has been collected. This study may also be stopped at any time by your physician or the Primary Investigator if it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.

Who can see or use my information? How will my personal information be protected?

If you decide to participate in this study, the study doctor and staff will collect medical and personal information about you as part of completing the study. We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. This study is being overseen by the Food and Drug Administration (FDA), therefore they may review your research records. The National Cancer Institute and associated agencies including the Cancer Immunotherapy Trials Network and the Division of Cancer Treatment and Diagnosis may also review your research records. Please refer to the information below which explains more specifically how your personal information will be protected.

What personal health information is collected and used in this study, and might also be disclosed?

The following personal health information will be collected and used for the purposes of this study.

- Name, date of birth, medical record number
- The history and diagnosis of your disease
- Specific information about any treatments you received, including previous treatment(s) you may have had and your response to them
- Information related to study visits and other tests/procedures performed while you are participating on this study.
- Information on side effects (adverse events) you may experience, and how these were treated
- Information about other medical conditions that may affect your treatment
- Medical data generated during this study- including physical exams, laboratory test results, and results of any other tests/procedures performed during the study

While collected as part of this study by your study doctor and study team, identifying information (including your name, address, telephone number, date of birth or any number/codes that will identify you [including medical record number]), will be kept as confidential as possible. It will not be sent outside of the University of Pennsylvania.

You will be assigned a unique subject registration number upon enrollment. This number and your initials will be used to identify you throughout the course of this study so that your identity is protected. The key to this code (which links your name back to the personal health information collected during this study) will be stored in a secure area and only the University of Pennsylvania study team will have access to this code.

It is possible that blood samples obtained from you as part of this study may be shared with other researchers, including those at for-profit organizations, but if this occurs, no information identifying you will be shared with the samples.

Why is your personal health information being used?

Your personal contact information is important for the research team to contact you during the study. Your personal health information and results of tests and procedures are being collected as part of this research study, and will be used to conduct and oversee this research study, and to help guide your medical treatment.

Which of our personnel may use or disclose your personal health information?

The following individuals may use or disclose your personal health information for this research study:

- The Principal Investigator and the Investigator's study team
- Authorized members of the workforce of the UPHS and the School of Medicine, and University of Pennsylvania support offices, who may need to access your

information in the performance of their duties (for example: for research oversight and monitoring, to provide treatment as part of this study or as part of your routine care, to manage accounting or billing matters, etc.). This includes members of the Institutional Review Board (IRB), an Ethics Committee at the University of Pennsylvania who are responsible for reviewing and overseeing research studies to ensure that they are safe and being well managed.

Who, outside of UPHS and the School of Medicine, might receive your personal health information?

As part of the study, the Principal Investigator, the study team and others listed above, may disclose your study-related records, including the results of the research study tests and procedures, to those listed below. In all disclosures outside of the University of Pennsylvania Health System and School of Medicine, you will not be identified by name, medical record number, address, telephone number, or any other direct personal identifier unless disclosure of the direct identifier is required by law. In records and information disclosed outside of the University of Pennsylvania Health System and School of Medicine, you will be assigned a unique code number.

Individuals or organizations responsible for supporting this study:

- Funding from the state of Pennsylvania will be used to provide support for this study.
- Other funding may be made available from the Abramson Cancer Center

Regulatory and safety oversight organizations

- The Food and Drug Administration
- DHHS (Department of Health and Human Services)
- Other regulatory agencies and/or their designated representatives in the United States and other countries
- The Cancer Center's Data Safety and Monitoring Committee

Once your personal health information is disclosed to others outside of UPHS or the School of Medicine, it may no longer be covered by federal privacy protection regulations.

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to University of Pennsylvania procedures developed to protect your privacy.

How long may UPHS and the School of Medicine be able to use or disclose your personal health information?

Your authorization for use of your personal health information for this specific study does not expire. If you sign this form, we will collect your health information until the end of the research study. We may collect some information from your medical records even after you finish taking part in this study. We will keep all of the information forever in case we need to look at it again. We will protect this information and keep it confidential.

Your information may be held in a research database. However, UPHS and the School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization to do so
- The University of Pennsylvania's Institutional Review Board grants permission after ensuring that appropriate privacy safeguards are in place
- As permitted by law

The data from this study may be published in the medical literature; however you will not be personally identified in any publication. Your identity will remain confidential unless disclosure is required by law.

Can you change your mind?

You have the right to withdraw your permission for the use of your personal health information, but if you do so, you must stop taking part in this study. You must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, your personal health information that was collected before we received your written request may still be used and disclosed, as necessary for the study. If you withdraw your permission to use your personal health information, you will also be withdrawn from the research study and no new information will be collected.

Will you be able to access your research records?

You have the right to see and get a copy of your medical records kept by the University of Pennsylvania. However, you will not be able to review or receive some of your records related to the research study until after the entire study has been completed.

By signing this document you are permitting the UPHS and the School of Medicine to use and disclose personal health information collected about you for research purposes as described above.

What is an Electronic Medical Record?

An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record.

If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient) and are participating in a University of Pennsylvania research study, results of research-related procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS.

If you have never received care within UPHS and are participating in a University of Pennsylvania research study that uses UPHS services, an EMR will be created for you for the purpose of maintaining any results of procedures performed as part of this research study. The creation of this EMR is required for your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that

would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have). Results of research procedures performed as part of your participation in the study (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in this EMR.

Once placed in your EMR, these results are accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by UPHS to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc).

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs with any question, concerns or complaints at the University of Pennsylvania by calling (215) 898-2614.

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania to disclose that personal health information to outside organizations or people involved with the operations of this study.

A copy of this consent form will be given to you.

_____	_____	
Name of Subject (Please Print)	Signature of Subject	Date
_____	_____	
Name of Person Obtaining Consent (Please Print)	Signature	Date

IRB Approved from: 03/10/2016 to: 01/07/2017