Informed Consent Form

Winship4463-18: A Phase Ib/II Trial of Siltuximab and PDR001 in Metastatic Pancreatic Cancer

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EMORY | WINSHIP CANCER INSTITUTE
A Cancer Center Designated by the National Cancer Institute

You Are Being Asked to Be in a Research Study
Concise presentation of key concepts

You are being asked to be in a research study. A research study is designed to answer a scientific question. If you agree to be in the study you will be one of 42 people who are being studied at Emory.

Why is this study being done?
This study is being done to answer the question: will combining two research drugs spartalizumab (also known as PDR001) and siltuximab (also known as Sylvant) in patients be safe and tolerable? You are being asked to be in this research study because you have metastatic pancreatic cancer.

Do you have to be in the study?
It is your decision to be part of this research study. You do not have to be in it. Your choice will not affect your access to medical care for your condition. Before you make your decision, you should take time to learn about the study.

What do I have to do if I choose to participate in this study?
If you are eligible and want to be part of the study, you will participate for about 2 years. The researchers will ask you to do the following: physical examination with measurement of your vital signs, an electrocardiogram (EKG), blood samples drawn, record concomitant medications, scans (CT or MRI) performed. Intravenous infusion of spartalizumab and siltuximab every 3 weeks. Patients will receive two research tumor biopsies. Some of these procedures will be paid for by the study.

How is this study going to help you?
If you are in the study, you will be helping the researchers answer the study question.

What are the risks or discomforts I should know about before making a decision?
The study will take time. The drug that is being tested may not work any better than regular care, and may even cause harm. All studies have some risks. Some risks are relatively small, like being bored or losing time. Some are more serious – for this study, these include: anaphylactic reaction (generalized allergic reaction), elevations in

cholesterol (lipid parameters), increased liver enzyme (protein) levels may be seen in the blood, bowel inflammation (colitis), optic neuritis, loss of privacy, and breach of confidentiality. A full list of expected risks, their frequency and severity are in the "What are the possible risks and discomforts?" section of this document.

Alternatives to Joining This Study

If you decide not to enter this study, there is care available to you outside of this research study. These options include other clinical trials or standard chemotherapy drugs approved for pancreatic cancer including liposomal irinotecan, gemcitabine, 5FU, oxaliplatin, irinotecan, or nab-paclitaxel for pancreatic cancer. The study doctor will discuss these with you. You do not have to be in this study to be treated for your cancer.

Costs

You WILL have to pay for some of the study procedures, in particular those that are not covered by your medical insurance.

The study team can help you work out how much you might have to pay. There is more information in the cost section below.

What Should I Do Next?

Read this form, or have it read to you. Make sure the study doctor or study staff explains the study to you. Ask questions (e.g., about exact time commitment, about unfamiliar words, more details on specific procedures, etc.) Make sure you understand which parts of these are research and which are standard care that you would have even if you did not join the study. Take time to consider this, and talk about it with your family and friends.

Emory University and Saint Joseph's Hospital
Consent to be a Research Subject / HIPAA Authorization

Title: Winship 4463-18: Phase II trial of Siltuximab and Spartalizumab in Metastatic Pancreatic Cancer

Principal Investigator: Maria Diab, MD

Investigator-Sponsor: Maria Diab, MD

Study-Supporters: Novartis, EUSA and NIH (National Institutes of Health)

Introduction

You are being asked to be in a medical research study. This form is designed to tell you everything you need to think about before you decide if you want to be a part of the study. **It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study.** The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.

Before making your decision:

- Please carefully read this form or have it read to you
- Please listen to the study doctor or study staff explain the study to you
- Please ask questions about anything that is not clear

You can take a copy of this consent form, to keep. Feel free to take your time thinking about whether you would like to participate. You may wish to discuss your decision with family or friends. Do not sign this consent form unless you have had a chance to ask questions and get answers that make sense to you. By signing this form you will not give up any legal rights.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This Web site will not include information that can identify you. At most the Web site will include a summary of the results. You can search this Web site at any time.

What is the purpose of this study?

The purpose of this study is to define the safety and tolerability of combining two research drugs spartalizumab (also known as PDR001) and siltuximab (also known as Sylvant) in patients with pancreatic cancer. Spartalizumab is not approved by the U.S. Food and Drug Administration (FDA) for pancreatic cancer. Siltuximab has been approved in the United States for the treatment of patients with multicentric Castleman's disease who are human immunodeficiency virus (HIV) negative and human herpesvirus-8 (HHV-8) negative. Some of the patients have been treated with siltuximab alone for up to 7 years and still continue to receive treatment. Siltuximab has not been approved by the U.S. Food and Drug Administration (FDA) for pancreatic cancer. The combination of siltuximab and spartalizumab is also investigational.

We plan to enroll up to 42 patients on this study. The trial has two parts. You are being considered for the second part of the study. In the first part, we will enroll up to 24 patients. The purpose of the

second phase is to determine the activity of siltuximab that can be given with spartalizumab. Patients will receive spartalizumab and siltuximab every three weeks. During the first 21 days (cycle 1) patients will be randomly assigned to receive either spartalizumab only or in combination of siltuximab. After cycle 1 is completed everybody on the study will receive the combination.

What will I be asked to do?

All subjects must sign an informed consent document prior to the initiation of any study related procedures. The informed consent document must be signed within 28 days of Cycle 1 Day 1.

Screening procedures (with the exception of the scans) are to be conducted within 28 days of starting the study (Cycle 1 Day 1).

- Review of study eligibility criteria
- Medical History
- Record concomitant medications taken up to 28 days prior to day 1 cycle 1
- Vital signs [temperature, heart rate (HR), blood pressure (BP) and respiratory rate (RR)]
- Physical Examination, including height and weight
- ECOG Performance Status evaluation (within 10 days or less of cycle 1 day 1)
- Laboratory Assessments- blood tests volume collected is around 40 mL.
    - Hematology: hemoglobin, hematocrit, red blood cell count, white blood cell count with differential and platelet count
    - Serum chemistry: sodium, potassium, chloride, bicarbonate, magnesium, calcium, phosphorus, blood urea nitrogen, creatinine, total bilirubin, Lactic Acid Dehydrogenase (LDH), total protein, Alkaline Phophatase (ALP), Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), uric acid and albumin. Fasting glucose.
    - Serum or urine pregnancy test for women of childbearing potential
    - Prothrombin time (PT) and activated partial thromboplastin time (aPTT)
    - Tumor markers(when applicable such as known elevated tumor markers): CA19-9
    - Thyroid function tests: Tri-iodothyronine (T3), Free Thyroxine (FT4), Thyroid Stimulating Hormone (TSH)
    - Hepatitis: HBV-DNA, Hepatitis B surface antigen (HBsAg), Hepatitis B core antibody (HBcAb), Hepatitis B surface antibody (HBsAb), HCV RNA- PCR
    - HIV, if clinically indicated
    - Blood sample 20 mL for correlative work
- Urinalysis (urine sample)
- 12-lead ECG
- Radiologic imaging studies to evaluate tumor status. Contrast computed tomography (CT) or magnetic resonance imaging (MRI) of the chest and abdomen and pelvis. Additional imaging may be obtained as clinically indicated. Baseline scans may be done within 8 weeks prior to cycle 1 day 1.

- Baseline fresh biopsy will be obtained with 28 days of day1 cycle 1 and after consent is signed.

Day 1 (±3 days) of each cycle

- Record concomitant medications
- Vital signs (temperature, HR, BP and RR)
- History and physical exam
- Laboratory Assessments- blood tests volume 20 -40 mL
    - Hematology hemoglobin, hematocrit, red blood cell count, white blood cell count with differential and platelet count
    - Chemistry sodium, potassium, chloride, bicarbonate, magnesium, calcium, phosphorus, blood urea nitrogen, creatinine, glucose (random), total bilirubin, LDH, total protein, ALP, ALT, AST, and albumin
    - Tumor markers - when applicable
    - T3, FT4, TSH cycle 2 and then after every 3rd cycle
    - Uric acid every other cycle
    - For the cycle1 day 1 laboratory assessments, blood samples from the screening tests may be used if completed within 1 week of day 1
- Blood sample 20 mL for correlative work (only cycle 1, 2, 3)
- Spartalizumab and siltuximab will be administered as IV infusion every 3 weeks. Given the variability of infusion pumps, a window of -10 minutes and +10 minutes is permitted.

Days 8 and 15 (±1 day) in cycle 1 and 2 ONLY

- Record concomitant medications
- Vitals (temperature, HR, BP and RR)
- History and physical exam
- Blood sample 20 cc for correlative work (only cycle1)
- Laboratory Assessments –Blood tests volume 20 to 30 mL
    - Chemistry sodium, potassium, chloride, bicarbonate, magnesium, calcium, phosphorus, blood urea nitrogen, creatinine, glucose (random), total bilirubin, LDH, total protein, ALP, ALT, AST, and albumin

Between days 14 and 21 of cycle 1

Repeat biopsy will be performed

Every month

Pregnancy test for women of child bearing potential

Every 3 cycles between day 15 and 21

- **Repeat cross sectional imaging (CT or MRI)**

End of treatment visit

- Vital signs (temperature, HR, BP and RR)
- History and physical exam
- Laboratory Assessments - Blood tests - volume *20-40* mL

- Hematology hemoglobin, hematocrit, red blood cell count, white blood cell count with differential and platelet count
- Chemistry sodium, potassium, chloride, bicarbonate, magnesium, calcium, phosphorus, blood urea nitrogen, creatinine, glucose (random), total bilirubin, LDH, total protein, ALP, ALT, AST, and albumin
- Tumor markers - when applicable
- T3, FT4, TSH cycle 2 and then after every 3rd cycle
- Blood sample 20 mL for correlative work

Safety Follow-Up Visit

You will be followed for at least 150 days after the last dose of study drug. In the first follow-up at 30 days the following will be performed.

- Vital signs (temperature, HR, BP and RR)
- History and physical exam
- Record concomitant medications
- Laboratory Assessments - Blood tests - volume *20-40* mL
  - Hematology hemoglobin, hematocrit, red blood cell count, white blood cell count with differential and platelet count
  - Chemistry sodium, potassium, chloride, bicarbonate, magnesium, calcium, phosphorus, blood urea nitrogen, creatinine, glucose (random), total bilirubin, LDH, total protein, ALP, ALT, AST, and albumin
  - Tumor markers - when applicable
  - T3, FT4, TSH

The study doctor or staff will discuss with you when and on which days to report to the clinic for the follow-up visits. If you have ongoing side effects from therapy, you will be seen at least every 8 weeks until side effect resolve. The following will be performed.

- Vital signs (temperature, HR, BP and RR)
- History and physical exam
- Record concomitant medications
- Laboratory Assessments - Blood tests - volume *20-40* mL
  - Hematology hemoglobin, hematocrit, red blood cell count, white blood cell count with differential and platelet count
  - Chemistry sodium, potassium, chloride, bicarbonate, magnesium, calcium, phosphorus, blood urea nitrogen, creatinine, glucose (random), total bilirubin, LDH, total protein, ALP, ALT, AST, and albumin
  - Tumor markers - when applicable
  - T3, FT4, TSH

If you stop taking the study drug before your cancer gets worse you will continue to come in for a follow-up visit every 9 weeks (+/- 1 week) until your cancer gets worse or you start a new treatment for your cancer. The imaging time point will occur every 9 weeks (± 7 days).

If at any time after you complete your treatment your cancer gets worse, or you start a new cancer treatment, you will be contacted by telephone every 12 weeks for survival follow-up until the study ends.

Subjects who are eligible for retreatment may have up to two safety follow-up visits, one after the Treatment Period and one after the Second Course Phase.

How will my medicine be provided?
The medicine that you will take will be dispensed by the pharmacy and delivered to the principal investigator or study team member. The principal investigator or health care providers on his/her research team will provide the medicine to you. If you have questions about the medicine, you should ask the principal investigator or study nurse. You may also call the pharmacy if you have questions about the medicine. The number for the pharmacy is included on your medicine package.

Who owns my study information and samples?
If you join this study, you will be donating your samples and study information. You will not receive any compensation if your samples or information are used to make a new product. If you withdraw from the study, data and samples that were already collected may be still be used for this study.

What are the possible risks and discomforts?
There may be side effects from the study drug or procedures that are not known at this time.

Siltuximab
The possible discomforts, side effects, and risks related to siltuximab treatment are not all known. Most side effects are not serious. Some may be serious and may require treatment or additional testing. Side effects seen on research studies can result from a patient's disease, the experimental drug, other drugs, other diseases, or a combination of these. These side effects may or may not have been due to siltuximab.

As of 23 July 2014, approximately 1,300 subjects had been enrolled in 15 research studies with siltuximab. About 890 subjects received siltuximab alone or together with other treatments, often chemotherapy. Of these subjects about 510 are known to have received siltuximab alone (including 140 healthy volunteers).

New side effects may happen. You will be watched closely, including through blood tests, and you will receive appropriate care if side effects happen. Please tell your study doctor if you have any of the side effects described below or any other ones not listed. You will be told of any new findings that may affect your decision to continue in this study.

The side effects related to siltuximab are based on 370 subjects who received siltuximab alone excluding the healthy volunteers treated siltuximab in a much lower dose. This section describes which and how frequently side effects occurred in these subjects who were treated with siltuximab alone. The following terms are used:

Very Common (affects more than 1 user in 10):

- Upper respiratory tract infection, an infection of the upper part of the respiratory tract such as nose, throat, sinuses, and airways
- Low platelet count, a type of blood cell that helps blood to clot. This can increase the risk of bleeding and bruising.
- Abdominal pain

- Low count of neutrophils, a type of white blood cell that helps to fight infections. This means that there could be a greater chance of getting an infection. Siltuximab could hide signs and symptoms of an infection such as fever. If you have an infection now or have a history of frequent infections, or if you feel sick even if you do not have a fever you should tell your study doctor right away.
- Itchy skin (pruritus)

Common (affects 1 to10 users in 100):

- Hypertension or high blood pressure
- Common cold (nasopharyngitis)
- Increased blood levels of a type of fat called triglycerides. High triglyceride levels may increase the risk for heart disease. This can be treated but blood tests are needed to look for it.
- Some decrease in the function of your kidneys called renal impairment. A medical condition in which your kidneys may not completely filter waste products from the blood. This can be detected by a blood test.
- A type of skin rash called maculo-papular rash, a rash with small bumps.
- Localized edema, localized swelling through retaining water
- Increased weight

Uncommon (affects 1 to 10 users in 1,000):

- Anaphylactic reaction is a severe allergic reaction that is sometimes seen when protein drugs are given. Your study doctor and their staff will be ready to treat such a reaction in case it happens. If this happens, you will not receive any more siltuximab infusions. You may not be able to be treated again with this type of medication. In the future, you should tell any other doctor you visit that you received siltuximab in this research study and if you had an allergic reaction

Precautions (safety measures)

- If you have an infection now or have a history of frequent infections, or if you feel sick even if you do not have a fever, you should tell your study doctor right away. Since siltuximab may mask a fever and could lower the level of neutrophils. Infections should be treated prior to siltuximab treatment.
- You should not receive live, attenuated vaccines for 4 weeks before the first dose of siltuximab, during the study and within 4 weeks after last administration of siltuximab, because possible risks are not known. Vaccines help protect people from certain illnesses. Examples of live, attenuated vaccines include the nasal influenza vaccine (FluMist®); measles, mumps, rubella (MMR) vaccine; oral polio vaccine; and varicella (chicken pox) vaccine.
- In addition to increase in triglycerides, elevations in cholesterol (lipid parameters) can also occur in patients treated with siltuximab. This should be managed according to current clinical guidelines for management of hyperlipidemia
- Increased liver enzyme (protein) levels may be seen in the blood. This may mean there is inflammation or damage in the liver.
- Holes (perforations) in the lining of the stomach or intestines may occur. This has been reported in 3 patients receiving siltuximab. Two of them died. These patients had other risk factors which may have caused the holes, including their disease (colon and ovarian cancer), abdominal surgery and a previous cancer drug they received. If you have stomach pain while on study, call your study doctor right away

Using Other Medicines

Siltuximab may affect the way some medicines work, including those listed below. The dose of these medicines may need to be adjusted during the course of the trial. You should tell your doctor about all the prescription and over-the-counter medicines and supplements you are taking so your doctor can advise you.

- atorvastatin, used to reduce cholesterol levels
- calcium channel blockers, such as amlodipine, used to treat high blood pressure
- theophylline, used to treat asthma
- warfarin, used to prevent blood clots
- phenytoin, used to treat seizures
- cyclosporine, used to block the immune system during organ transplants
- benzodiazepines, such as temazepam, used to relieve anxiety
- oral contraceptives, used to prevent pregnancy

Side effects of **spartalizumab (PDR001)** include:

Based on the mechanism of action, medicines like PDR001 can cause your immune system to attack normal organs and tissues in various areas of your body and can affect the way they work.

Side effects observed in clinical use with medicine blocking PD-1 in humans typically involve the skin (e.g. rash, itching), intestine (e.g. diarrhea, abdominal pain, bowel inflammation), lungs (e.g. shortness of breath, cough, lung inflammation), hormonal glands (including inflammation and malfunction of the pituitary, thyroid, and adrenal glands or pancreas/diabetes), inflammation of the liver and kidney (resulting in poor function). However, any organ in the body can be affected, rarely including the heart, muscles, blood vessels and blood cells, eyes, nerves or brain. Furthermore, complications in patients who have previously received a bone marrow or solid organ transplant have been reported (e.g. organ rejection, severe graft-versus-host disease).

These side effects are mostly mild or moderate in severity, however, can be severe or life-threatening, and rarely lead to death in certain cases. These problems may happen anytime during treatment or even after your treatment has ended, and might require prolonged treatment with medications to reduce the activity of the immune system or hormonal replacement.

Based on pooled safety data from 513 cancer patients treated with single agent PDR001 across four clinical research studies, observed side effects thought to be caused by PDR001 include:

Organ	Side effect	Frequency	*No. of patients (%)*	Possible signs and symptoms
Hormone glands	Increased blood sugar	Common	*24 (4.7%)*	Excessive thirst or lots of urine
	Low thyroid function (hypothyroidism)	Common	*40 (7.8%)*	Feeling tired or cold, weight gain or loss, constipation, rapid or irregular heartbeat, sweating, irritability, tremor, eyesight changes, headaches, weakness, confusion, hallucinations, memory loss, labile mood, insomnia, feeling less hungry
	High thyroid function (hyperthyroidism)	Common	*15 (2.9%)*	
	Thyroid gland inflammation (thyroiditis)	Uncommon	*3 (0.6%)*	
	Pituitary gland inflammation (hypophysitis)	Uncommon	*1 (0.2%)*	
Stomach and intestine	Nausea	Very common	*98 (19.1%)*	
	Constipation	Very common	*79 (15.4%)*	

Organ	Side effect	Frequency	*No. of patients (%)*	Possible signs and symptoms
	Diarrhea	Very common	*71 (13.8%)*	
	Vomiting	Very common	*66 (12.9%)*	
	Dry mouth	Common	*20 (3.9%)*	
	Bowel inflammation (colitis)	Uncommon	*3 (0.6%)*	Loose stools or more bowel movements than usual, severe abdominal pain or tenderness, blood in your stools or dark, tarry, sticky stools
General	Fatigue	Very common	*121 (23.6%)*	Feeling tired or weak
	Decreased appetite	Very common	*101 (19.7%)*	
	Fever	Very common	*82 (16%)*	
Liver	Abnormal liver tests:			Yellowing of your skin or the whites of your eyes, fever, nausea or vomiting, abdominal pain (on the right side of your stomach), drowsiness, dark urine, bleeding or bruising more easily than normal, feeling less hungry than usual, abnormal liver tests (indicative of potential liver damage)
	• AST increased	Common	*48 (9.4%)*	
	• Blood ALP increased	Common	*32 (6.2%)*	
	• ALT increased	Common	*27 (5.3%)*	
	• Hyperbilirubinemia	Uncommon	*1 (0.2%)*	
	Liver inflammation (hepatitis)	Uncommon	*1 (0.2%)*	
Muscle and joint	Joint pain	Common	*(>10.0%)*	
	Muscle pain	Common	*17 (3.3%)*	
	Joint inflammation	Uncommon	*3 (0.6%)*	Inflamed/painful joints or muscles, decreased range of motion of joint, joint swelling, muscle weakness
	Muscle inflammation	Uncommon	*1 (0.2%)*	
	Rheumatoid arthritis	Uncommon	*1 (0.2%)*	
Nervous System	Optic neuritis	Uncommon	*1 (0.2%)*	Changes in eyesight
	Myasthenia gravis	Uncommon	*1 (0.2%)*	Severe muscle weakness, can result in double vision, drooping eyelids, difficulty in walking, eating or speaking
Lung	Shortness of breath at rest or exertion (dyspnea)	Very common	*97 (18.9%)*	
	Lung inflammation (pneumonitis)	Common	*9 (1.8%)*	Cough (new or worsening), shortness of breath at rest or exertion, chest pain
Skin	Rash	Very common	*60 (11.7%)*	Rash, dry skin, itching or burning skin, skin redness, skin darkening or changes in skin color, hair loss, hives, papules, pustules or blisters
	Itching (pruritus)	Common	*41 (8%)*	
	Skin redness (erythema)	Common	*7 (1.4%)*	
	Dry Skin	Common	*6 (1.2%)*	
	Skin discoloration (vitiligo)	Common	*6 (1.2%)*	
	Itching over the whole body	Uncommon	*4 (0.8%)*	
	Urticaria (hives)	Uncommon	*2 (0.4%)*	
	Dermatitis Acneiform	Uncommon	*2 (0.4%)*	
	Hair loss (alopecia)	Uncommon	*2 (0.4%)*	
	Dermatitis allergic	Uncommon	*1 (0.2%)*	
	Lichen planus	Uncommon	*1 (0.2%)*	
	Darkening of the skin (hyperpigmentation)	Uncommon	*1 (0.2%)*	
Immune system	Anaphylactic reaction (generalized allergic reaction)	Uncommon	*1 (0.2%)*	Chills, itching or rash, difficulty breathing, dizziness, fever, nausea, vomiting, or flushing

Immune-related endocrinopathies (hormone related side effects in the above table) are frequently permanent and would require life-long hormone replacement. Autoimmune diabetes is possible and that may lead to life-long insulin therapy. Categories are based on the following conventions: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000)

Infusion of drugs such as PDR001 can sometimes cause reactions most commonly during the first infusion. Infusion reactions usually consist of symptoms such as fever, chills, nausea, vomiting, headache, dizziness, shortness of breath, low blood pressure, rash or itching, and weakness. So far, infusion reactions have been uncommon with PDR001.

PDR001 is an investigational drug being tested and thus not all of the possible side effects that may occur from taking the drug are known at this time. The expected side effects listed in this form may vary from person to person, and you may experience other side effects that are not listed in this form. At each visit, the Study Doctor will ask you about any unusual symptoms. You should discuss all of them with the Study Doctor. You will be checked regularly for new or worsening side effects. This may require extra visits and examinations including blood tests.

You will be given any new information as it becomes available that can help you choose whether to continue in the study.

Single agent treatment with either study drug is unlikely to have adequate anti-tumor activity. If one of the two agents (siltuximab or spartalizumab) is permanently discontinued due to side effects, you may be able to receive single-agent therapy for a period of time with the other agent only in the following conditions: if there is evidence of benefit from the treatment after discussion with your physician or if there are adverse reactions due to spartalizumab that may benefit from continuing siltuximab.

What effects could the tests have on me?

Electrocardiogram (ECG): May cause minimal discomforts during the attachment and removal of the ECG leads to and from the skin.

Contrast Agents: Your CT or MRI procedure will require the use of a "contrast agent." The contrast agent is a substance that helps the radiologist interpret the images. The contrast agent will be injected by either a hand-held needle or a machine that does the injection. Most contrast agents stay in your body for only a few minutes, but some of them can remain for a few hours or days without any harm to you or anyone near you. Contrast agents are generally quite safe, but any injection involves some risks. The injection could harm a nerve, artery or vein, or cause infection. The contrast agent could affect kidney function or cause an allergic reaction, though these outcomes are rare. The contrast agent could also leak from your veins a little causing swelling and discomfort, that is typically treated with ice packs.

Magnetic Resonance Imaging (MRI): MRI exams use powerful magnets to create images of the body. In addition to the possible reactions to contrast materials, you may feel claustrophobic while in the magnet, and will hear loud beeping or hammering noises. If you have tattoos or any metal items in your body such as implants, pacemakers, clips or shrapnel, we will do special screening to make sure your MRI scan is done safely.

Radiation-Related Risks: You will be exposed to radiation from CT scans. These procedures are necessary for your medical care and will occur even if you do not participate in this study. The radiation dose estimate that you will receive is equal to or less than the radiation exposure allowed to be received by a radiation worker for 6 years. The principal risk associated with a radiation dose is the possibility of developing a radiation-induced cancer later in life. Although the risk from radiation is cumulative it is not expected to adversely affect your condition or treatment. The Emory University Radiation Safety Committee has reviewed and approved the use of radiation in this research study.

Tumor Biopsy: Biopsies will be obtained under CT scan guidance. Biopsies will involve areas were cancer is safely accessible including liver. Discussion regarding potential risks of biopsies will be performed prior to the biopsy after determining site of biopsy. Having biopsies performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling and/or infection at the site of the biopsy, perforation of gastric wall/esophagus and rarely, death. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site. Other potential risks will be described to you and discussed with you by physicians who conduct these biopsies.

The effect of siltuximab or spartalizumab on human sperm, pregnant women, breastfeeding women, unborn babies, or nursing infants is not known. Pregnant women and breastfeeding women cannot participate in this study. Females of child bearing potential must have a pregnancy test when beginning this study and monthly while on study that shows they are not pregnant.

It is very important that women taking part in this study do not become pregnant while taking part in this study. During this study and for 150 days after the last dose of study drug, women of childbearing potential and men must use proven birth control methods. Your study doctor will discuss effective birth control methods with you. Men must not donate sperm and women must not donate eggs during the study and for 150 days after the last dose of study drug.

If you think that you have become pregnant or may have fathered a child while taking part in the study, you must tell your study doctor immediately. You should also notify your childbirth doctor that the mother/father received an experimental drug (spartalizumab and siltuximab).

If you are a female study patient and you become pregnant during your participation in this study, your treatment with study drug will be stopped and you may be withdrawn from some of the study procedures but not from follow-up by your study doctor. The study doctor will ask for your permission to stay in contact with you throughout the length of the pregnancy.

If you are a male study patient and you father a child during your participation in this study, the study doctor will ask for your partner's permission to stay in contact with her throughout the length of pregnancy.

Will I benefit directly from the study?

Your cancer may improve while you are in this study but it may not, and it may even get worse. This study is designed to learn more about the safety of the combination of siltuximab and spartalizumab. The study results may be used to help others in the future.

Will I be compensated for my time and effort?

There will be no compensation for participation in the trial.

What are my other options?

If you decide not to enter this study, there is care available to you outside of this research study. These options include other clinical trials or standard chemotherapy drugs approved for pancreatic cancer including liposomal irinotecan, gemcitabine, 5FU, oxaliplatin, irinotecan or nab-paclitaxel for pancreatic cancer. In addition patients with microsatellite instable (mismatch repair deficient or MSI-H) pancreatic cancer also have an option of pembrolizumab which is FDA approved for this

indication. The study doctor will discuss these with you. You do not have to be in this study to be treated for your cancer.

Taking part in this study, however, may make you unable to participate in some other research studies, if they exclude people who have taken certain treatments. You should discuss this with the researchers if you have concerns. You may wish to research other study options at websites like clinicaltrials.gov and ResearchMatch.org.

How will you protect my private information that you collect in this study?

Whenever possible, a study number, rather than your name, will be used on study records. Your name and other identifying information will not appear when we present or publish the study results.

Study records can be opened by court order. They also may be provided in response to a subpoena or a request for the production of documents.

Certificate of Confidentiality

There is a Certificate of Confidentiality from the National Institutes of Health for this Study. The Certificate of Confidentiality helps us to keep others from learning that you participated in this study. Emory will rely on the Certificate of Confidentiality to refuse to give out study information that identifies you. For example, if Emory received a subpoena for study records, it would not give out information that identifies you.

The Certificate of Confidentiality does not stop you or someone else, like a member of your family, from giving out information about your participation in this study. For example, if you let your insurance company know that you are in this study, and you agree to give the insurance company research information, then the investigator cannot use the Certificate to withhold this information. This means you and your family also need to protect your own privacy.

The Certificate does not stop Emory from making the following disclosures about you:

- Giving state public health officials information about certain infectious diseases,
- Giving law officials information about abuse of a child, elderly person or disabled person.
- Giving out information to prevent harm to you or others.

Giving the study sponsor or funders information about the study, including information for an audit or evaluation.

Storing and Sharing your Information

De-identified data from this study, including your de-identified genetic information, may be shared with the research community at large to advance science and health. Data from this study may be placed into public databases where, in addition to having no direct identifiers, researchers will need to sign data use agreements before accessing the data. We will remove or code any personal information that could identify you before your information is shared. This will ensure that, by current scientific standards and known methods, it is extremely unlikely that anyone would be able to identify you from the information we share. Despite these measures, we cannot guarantee anonymity of your personal data.

Blood collected for research purpose as part of this study may be stored for future use in research on pancreatic cancer or other cancers.

How is my Genetic Information Protected? What are the Risks?

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

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

Be aware that GINA does **not** protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance, and does not apply to employers with less than 15 employees.

In addition to GINA, the State of Georgia has laws that prohibit insurers from using genetic testing information for any non-treatment purpose. However, like GINA, this state law protection has exclusions: life insurance policies, disability income policies, accidental death or dismemberment policies, Medicare supplement policies, long-term care insurance policies, credit insurance policies, specified disease policies, hospital indemnity policies, blanket accident and sickness policies, franchise policies issued on an insurance policy written as a part of workers' compensation equivalent coverage, or other similar limited accident and sickness policies.

Privilege

In the State of Georgia, in some circumstances your genetic information has may have special legal protections called "privilege." This means that the information cannot be used as evidence in a court. By allowing us to use and disclose your genetic information for this research study along with other information about you that genetic information used in the research may no longer have that legal protection. Other protections described in this form will still apply. There are also other confidentiality protections for research data in general under Georgia state law.

Medical Record

If you have been an Emory and Saint Joseph's Hospital patient before, then you already have an Emory and Saint Joseph's Hospital medical record. If you have never been an Emory and Saint Joseph's Hospital patient, you do not have one. An Emory and Saint Joseph's Hospital medical record will be made for you if an Emory and Saint Joseph's Hospital provider or facility gives you any services or procedures for this study.

Copies of the consent form/HIPAA authorization that you sign will be put in any Emory and Saint Joseph's Hospital medical record you have now or any time during the study.

Emory and Saint Joseph's Hospital may create study information about you that can help with your care. For example, the results of study tests or procedures. These study results will be put in your Emory and Saint Joseph's Hospital medical record. Anyone who has access to your medical records

will be able to have access to all the study information placed there. The confidentiality of the study information in your medical record will be protected by laws like the HIPAA privacy rule. State and federal laws may not protect the research information from disclosure.

Tests and procedures done at non-Emory and Saint Joseph's Hospital places may not become part of your Emory and Saint Joseph's Hospital medical record. Also, if you decide to be in this study, it is up to you to let your other health providers know.

In Case of Injury

If you get ill or injured from being in the study, Emory and Saint Joseph's Hospital will help you to get medical treatment. Emory and Saint Joseph's Hospital and the sponsor have not, however, set aside any money to pay you or to pay for this medical treatment. The only exception is if it is proven that your injury or illness is directly caused by the negligence of an Emory and Saint Joseph's Hospital or sponsor employee. "Negligence" is the failure to follow a standard duty of care.

If you become ill or injured from being in this study, your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurer does not pay, then you will have to pay these costs.

If you believe you have become ill or injured from this research, you should contact Dr. Maria Diab at telephone number [redacted]. You should also let any health care provider who treats you know that you are in a research study.

Novartis (drug supplier) will not pay any money to you or your medical bills.

Costs

The study supporter will pay for certain items and services that you may receive if you take part in this study.

Siltuximab and spartalizumab will be free of charge. Paired biopsies will be free of charge.

You will have to pay for the items or services for which the study supporter does not pay. The supporters will not pay for your regular medical care. If you have insurance, Emory and Saint Joseph's Hospital will submit claims to your insurance for items and services that the supporter does not cover. Emory and Saint Joseph's Hospital will send in only those claims for items and services that it reasonably believes your insurance will pay and that the supporter has not paid.

The actual amount that you have to pay depends on whether or not you have health insurance and whether or not that insurance will pay for any research study costs. Generally, insurance companies will not pay for items and services that are required just for a research study. Some insurance companies will not pay for regular medical treatment or treatment for complications if you are in a study. How much you will have to pay for any co-payments, deductibles or co-insurance depends on your plan. Emory and Emory Saint Joseph's Hospital and the sponsor will not pay for these costs.

It is a good idea to contact your insurance provider and tell them you want to be in this research study. Ask them what they will pay for and what they will not pay for. You can also ask the study team for help in figuring out what you will have to pay.

If you do not have insurance, Emory and Emory Saint Joseph's Hospital will review your case as part of its program for low-income patient care. The standard policies of that program will apply. The program will figure out if you have to pay any costs for taking part in the study and what those costs will be.

Withdrawal from the Study
You have the right to leave a study at any time without penalty.

For your safety, however, you should consider the study doctor's advice about how to go off the study treatment. If you leave the study before the final planned study visit, the researchers may ask you to have some of the final steps done.

The researchers also have the right to stop your participation in this study without your consent for any reason, especially if they believe it is in your best interest or if you were to object to any future changes that may be made in the study plan.

Authorization to Use and Disclose Protected Health Information

The privacy of your health information is important to us. We call your health information that identifies you, your "protected health information" or "PHI." To protect your PHI, we will follow federal and state privacy laws, including the Health Insurance Portability and Accountability Act and regulations (HIPAA). We refer to all of these laws as the "Privacy Rules." Here we let you know how we will use and disclose your PHI for the main study and for any optional studies in which you may choose to participate.

Main Study

PHI that Will be Used/Disclosed:
The PHI that we will use or share for the main research study includes:

- Medical information about you including your medical history and present/past medications.
- Results of exams, procedures and tests you have before and during the study.
- Laboratory test results.

Purposes for Which Your PHI Will be Used/Disclosed:
We will use and share your PHI for the conduct and oversight of the research study. We will use and share your PHI to provide you with study related treatment and for payment for such treatment. We will also use and share your PHI to conduct normal business operations. We may share your PHI with other people and places that help us conduct or carry out the study, such as laboratories, data management centers, data monitors, contract research organizations, Institutional Review Boards (IRBs) and other study sites. If you leave the study, we may use your PHI to determine your health, vital status or contact information.

Use and Disclosure of Your Information That is Required by Law:
We will use and disclose your PHI when we are required to do so by law. This includes laws that require us to report child abuse or abuse of elderly or disabled adults. We will also comply with legal requests or orders that require us to disclose your PHI. These include subpoenas or court orders.

Authorization to Use PHI is Required to Participate:
By signing this form, you give us permission to use and share your PHI as described in this document. You do not have to sign this form to authorize the use and disclosure of your PHI. If you do not sign this form, then you may not participate in the research study or receive research-related treatment. You may still receive non-research related treatment.

People Who will Use/Disclose Your PHI:
The following people and groups will use and disclose your PHI in connection with the research study:

- The Principal Investigator and the research staff will use and disclose your PHI to conduct the study and give you study related treatment.
- Emory and Emory Saint Joseph's Hospital may use and disclose your PHI to get payment for study related treatment and to run normal business operations.
- The Principal Investigator and research staff will share your PHI with other people and groups to help conduct the study or to provide oversight for the study.
- Dr. Maria Diab is the Sponsor of the study. The Sponsor may use and disclose your PHI to make sure the research is done correctly and to collect and analyze the results of the research. The Sponsor may disclose your PHI to other people and groups like study monitors to help conduct the study or to provide oversight for the study.
- The following people and groups will use your PHI to make sure the research is done correctly and safely:
    - Emory and Emory Saint Joseph's Hospital offices that are part of the Human Research Participant Protection Program and those that are involved in study administration and billing. These include the Emory IRB, the Emory Research and Healthcare Compliance Offices, and the Emory Office for Clinical Research.
    - Government agencies that regulate the research including: Office for Human Research Protections and Food and Drug Administration
    - Government agencies in other countries where the study drug may be considered for approval
    - Public health agencies.
    - Research monitors and reviewer.
    - Accreditation agencies.
    - Drug Suppliers: Novartis, EUSA, and their authorized agents
    - NIH (National Institutes of Health)
- Sometimes a Principal Investigator or other researcher moves to a different institution. If this happens, your PHI may be shared with that new institution and their oversight offices. PHI will be shared securely and under a legal agreement to ensure it continues to be used under the terms of this consent and HIPAA authorization.

Optional Study for Storage of Specimens for Future Research

Authorization for This Use of PHI is Required to Participate in Optional Study, but Not in Main Study:
You do not have to authorize the use and disclosure of your PHI for the optional studies. If you do not authorize the use and disclosure of your PHI for the optional studies, then you may not participate in the optional research study, but you can still be in the main research study.

People Who Will Use/Disclose Your PHI for Optional Study:
The same people and groups who will use and disclose your PHI for the main study will also do so in connection with the optional research study

Expiration of Your Authorization
Your PHI will be used until this research study ends.

Revoking Your Authorization
If you sign this form, at any time later you may revoke (take back) your permission to use your information. If you want to do this, you must contact the study team at:

Maria Diab, MD
Winship Cancer Institute, Emory University
1365-C Clifton Road NE
Atlanta, GA 30322

At that point, the researchers would not collect any more of your PHI. But they may use or disclose the information you already gave them so they can follow the law, protect your safety, or make sure that the study was done properly and the data is correct. If you revoke your authorization you will not be able to stay in the study.

Other Items You Should Know about Your Privacy
Not all people and entities are covered by the Privacy Rules. HIPAA only applies to health care providers, health care payers, and health care clearinghouses. If we disclose your information to people who are not covered by the Privacy Rules, including HIPAA, then your information won't be protected by the Privacy Rules. People who do not have to follow the Privacy rules can use or disclose your information with others without your permission if they are allowed to do so by the laws that cover them. The study supporters, and people and companies working with the study supporters on this study are not covered by the Privacy Rules. They will only use and disclose your information as described in this Consent and Authorization.

To maintain the integrity of this research study, you generally will not have access to your PHI related to this research until the study is complete. When the study ends, and at your request, you generally will have access to your PHI that we maintain in a designated record set. A designated record set is data that includes medical information or billing records that your health care providers use to make decisions about you. If it is necessary for your health care, your health information will be provided to your doctor.

We may remove identifying information from your PHI. Once we do this, the remaining information will not be subject to the Privacy Rules. Information without identifiers may be used or disclosed with other people or organizations for purposes besides this study.

Contact Information
Contact: Dr. Maria Diab at [redacted]

- 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 drug, or
- if you have questions, concerns or complaints about the research

Contact the Emory Institutional Review Board at [redacted]:

- if you have questions about your rights as a research participant.
- if you have questions, concerns or complaints about the research.
- You may also let the IRB know about your experience as a research participant through our Research Participant Survey at http://www.surveymonkey.com/s/6ZDMW75.

Consent and Authorization

Consent and HIPAA Authorization for Optional Study/Studies:
Please initial below if you opt to participate in and authorize use and disclosure of your PHI in the optional study/studies previously described:

SAMPLES FOR FUTURE RESEARCH STUDIES

_____ I agree my samples and related information may be kept for use in future health research.

_____ I agree that my study doctor, or their representative, may contact me or my physician to see if I wish to participate in other research in the future.

TO BE FILLED OUT BY SUBJECT ONLY

Please **print** your name, **sign**, and **date** below if you agree to be in the main study. By signing this consent and authorization form, you will not give up any of your legal rights. We will give you a copy of the signed form to keep.

_____
Name of Subject

_____ _____ ____:____ am / pm
Signature of Subject (18 or older and able to consent) **Date** **Time (please circle)**

TO BE FILLED OUT BY STUDY TEAM ONLY

_____
Name of Person Conducting Informed Consent Discussion

_____ _____ ____:____ am / pm
Signature of Person Conducting Informed Consent Discussion **Date** **Time (please circle)**