FOX CHASE CANCER CENTER
TEMPLE HEALTH

FOX CHASE CANCER CENTER
AT TEMPLE UNIVERSITY HOSPITAL
All hospital services provided by Temple University Hospital

INFORMED CONSENT DOCUMENT

TH-113: Depletion of Myeloid Derived Suppressor Cells to Enhance anti-PD-1 Therapy

Principal Investigator: Martin J. Edelman, MD

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You should discuss your decision with your friends and family. You will also discuss it with your health care team. If you have any questions, you can ask your study doctor for more explanation.

You are being asked to take part in this research study because you have non-small cell lung cancer.

The sponsor-investigator of this study is Martin J. Edelman, MD at Fox Chase Cancer Center.

The study is supported by Bristol-Myers Squibb and Fox Chase Cancer Center.

Why is this research study being done?

The purpose of this research study is to see if MDSCs are altered in patients receiving Gemcitabine in combination with Nivolumab. MDSCs are a type cells that are thought to play a role in suppressing immune response against cancer. Nivolumab is an antibody (a type of human protein) that is being tested to see if it will allow the body's immune system to work against tumor cells. Gemcitabine is a drug that is already approved by FDA to treat patients with non-small cell lung cancer. The combination of nivolumab and gemcitabine is not yet approved for treating non-small cell lung cancer.

We do not know if you will benefit from this research study. It is possible that your condition will get better, but it is also possible that there will be no effect on your condition or that your condition will get worse. We can use what we learn from this research study to help other people with the same disease.

How many people will take part in this research study?

10 people will take part in this research study.

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

Before you begin the research study

You will need to have the following exams, tests or procedures to find out if you can be in the research study. These exams, tests or procedures are part of regular cancer care and may be done even if you do not join the research study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- We will ask you about your medical history and medicines you are taking
- We will do a physical exam which will include height, weight and vital signs
- We will ask about your ability to do your daily activities
- Routine blood tests (1 tablespoon)
- We will check your heart function by performing an EKG
    - EKG is a test to measure the electrical activity of your heart
- Blood for pregnancy test (2 teaspoon), if you are a female and able to become pregnant.
- We will evaluate your cancer by doing a CT scan
    - A CT scan is a computerized x-ray that gives your study doctor pictures of the inside of your body.
- A biopsy sample is required for entry in the study if a standard of care test for determining the expression of a biomarker is not already done. If you have the testing done we will request tissue sample from you but this is optional. A biopsy is a small piece of tissue from your cancer.

During the research study

Study Treatment

If the screening procedures show you can take part in the study, you will receive nivolumab intravenously over a period of 30 minutes on day 1 and then on day 15 of the treatment cycle. In addition, you will also receive gemcitabine intravenously over a period of 30 minutes on day 1, day 8 and day 15 of the treatment cycle. Gemcitabine will be administered before nivolumab administration. **Each treatment cycle is 28 days**. Once a treatment cycle ends the next treatment cycle will begin. If during the treatment your study doctor determines that you are having unacceptable side-effects due to nivolumab, you may receive only gemcitabine for the rest of the study.

Tests and Procedures

If the exams, tests and procedures show that you can be in the research study, and you choose to take part, then you will need the following tests and procedures. They are part of regular cancer care. Some of these tests are being done more often because you are in this research study.

- We will ask you about all the medicines you are taking
- We will do a physical exam which will include vital signs and weight
- We will ask about your ability to do your daily activities
- Routine Blood tests (1 tablespoon) – once every cycle.
- Blood for pregnancy test (2 teaspoons), if you are a female and able to get pregnant – once every cycle
- We will ask you about any side effects you may be experiencing.
- We will check your heart function by performing EKG, however this test will be performed only if your study doctor recommends.
- We will assess your tumor by performing a CT scan – once every 8 weeks
- Blood for research on day 1, 8, 15 of cycle 1, and day 1 of cycles 2, 3 (up to 1.5 tablespoons)
- Optional blood collection for future research and banking (1.5 tablespoon) – every other cycle starting from cycle 1.

If you experience any changes in your body or develop any new or worsening side-effects during or after the infusion of the study drug/s you should inform the study doctor or nurse immediately.

After you stop taking the study drug

Safety Follow-up

We will perform a safety follow-up 30 days after discontinuing the treatment. In this follow-up visit we will perform the following tests and procedures.

- We will ask you about the medicines that you are taking
- We will do a physical exam including weight and vital signs
- We will ask about your ability to do your daily activities
- Routine blood test (1 tablespoon)
- Optional blood for future research and banking (1.5 tablespoon).
- We will ask you about any side effects you may be experiencing

Follow-up

If you discontinued the study treatment due to reasons other than disease progression we would do follow-up visits to check the status of your disease. In this visit we will perform the following tests and procedures.

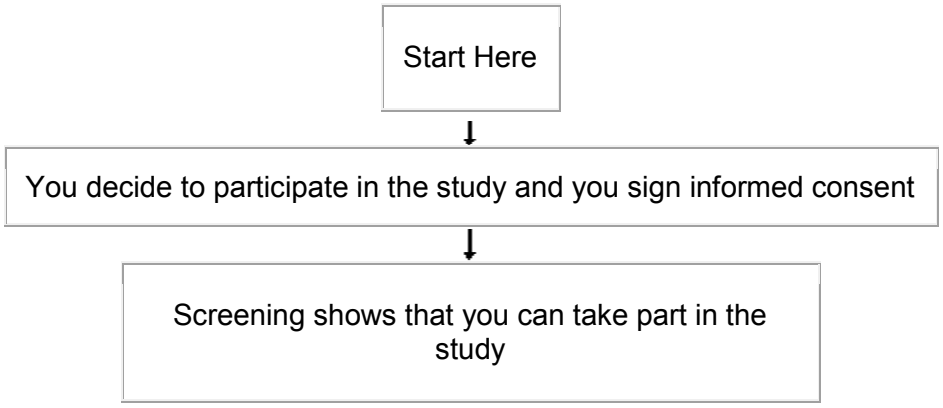
- We will ask you about the medicines that you are taking
- We will do a physical exam including weight and vital signs
- We will evaluate your cancer by doing a CT scan once every 8 weeks.
- We will ask you about any side effects you may be experiencing.

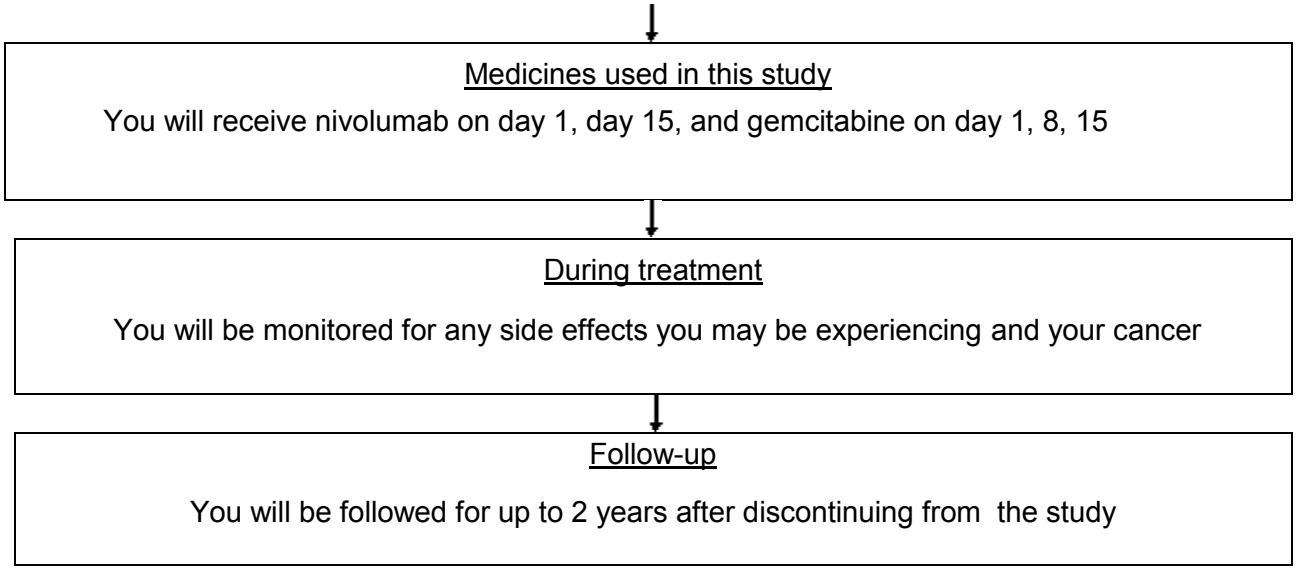
Long-term follow-up

We will follow-up via a phone call once every 3 months to check your overall health after it is confirmed that your disease has worsened (disease progression).

Study Plan

Another way to find out what will happen to you during the research study is to read the chart below. Start reading at the top and read down the list, following the lines and arrows.





How long will you be in the research study?

You will be asked to take the study drug/s as long you are benefiting from the treatment or your disease does not get worse. You will also be removed from the study if your doctor thinks that you have unacceptable toxicities due to the study drug/s and it is in your best interest that you stop participating in the study.

Can you stop being in the research study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely.

It is important to tell the study doctor if you are thinking about stopping so any risks due to the study nivolumab and/or gemcitabine can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what followup care and testing could be most helpful for you.

Can you be removed from this research study?

The study doctor may stop you from taking part in this research study at any time if he/she believes it is in your best interest; if you do not follow the research study rules; or if the research study is stopped.

What side effects or risks can you expect from being in the research study?

You may have side effects while on the research study. Everyone taking part in the research study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the nivolumab and/or gemcitabine. In some cases, side effects can be serious, long lasting, or may never go away. There is also a risk of death

You should talk to your study doctor about any side effects that you have while taking part in the research study.

Risks and side effects related to the **nivolumab** include those which are:

Likely (≥ 5%)

- Fatigue – feeling tired
- Skin reactions – including rash, itching, hives, redness, and dry skin
- Hyponatremia (low sodium levels in the blood) – symptoms may include nausea and vomiting, loss of appetite, headache, confusion, fatigue, restlessness and irritability, muscle weakness, spasms or cramps, decreased consciousness, seizures or coma.
- Diarrhea – increased frequency of bowel movements with loose, watery stools
- Nausea
- Abdominal pain
- Decreased appetite
- Anemia (low hemoglobin, low hematocrit or low red blood cell count) – red blood cells carry oxygen and nutrients throughout the body. Symptoms that may be experienced as a result of low red blood cell counts may include feeling tired and weak, shortness of breath, increased heart rate, dizziness or lightheadedness, headache, chest pain and pale skin.
- Fever
- Joint pain or stiffness

Less Likely (2-4%)

- Bowl inflammation
- Liver function blood test abnormalities
- Loss of color (pigment) from areas of skin
- Thyroid gland abnormalities
- Blood chemistry abnormalities, including low blood phosphate, magnesium, and potassium levels
- High blood uric acid level
- Dizziness
- Low white blood cells
- Pain in arms and legs
- Peripheral neuropathy – numbness and tingling in the hands and feet
- Allergic reaction during or between drug infusion
- Cough
- Dry Mouth
- Vomiting – throwing up
- Weight loss
- Headache
- Chills
- Muscle soreness, weakness, stiffness, spasms or paralysis
- Shortness of breath
- Abnormal taste
- Flushing
- High or low blood pressure
- Increased sensitivity of skin to sunlight
- Constipation
- Difficulty swallowing
- Heartburn
- Thrombocytopenia (low platelet count) – platelets are important in stopping bleeding. A low platelet count can increase the time to form a blood clot

- Pneumonitis (Lung inflammation – see below)

Lung Inflammation: It is possible that nivolumab may cause inflammation of the tissues of the lung. This adverse effect has been reported infrequently in patients treated with nivolumab. While many patients with x-ray or CT abnormalities have not developed any symptoms, some patients have developed mild to severe symptoms and in rare cases, death has occurred as a result of their lung inflammation.
Signs and symptoms of lung inflammation may include difficulty breathing, pain or discomfort while breathing, chest pain, cough, shortness of breath, increased rate of breathing, fever, low blood oxygen levels, or fatigue.
Your study doctor and nurse will watch you closely for changes in your ability to breathe and for other signs or symptoms that might show you are developing this type of lung inflammation and will perform regular tests including physical exams, measurement of oxygen levels through non-invasive testing (i.e., pulse oximeter), blood tests, chest x-rays and/or CT scans.

Please inform your study doctor or nurse <u>AT ONCE</u> if you experience any of the following:

- Any new or increased shortness of breath;
- Any new or increased chest pain;
- Any new or increased pain/difficulty while breathing;
- Any new or increased cough or any significant change in your type of cough; for example any new or increased mucous or blood in your cough;
- Any change in the amount of oxygen you require;
- Any fever, fatigue, or other symptoms that occur at the same time as any changes to your breathing or other lung symptoms.

If you start to develop symptoms, your study doctor will ask you to return to the clinic for additional tests, which could include a physical exam, measurement of oxygen levels, blood tests, chest x-rays, and/or CT scans. You will be monitored very closely for changes in your overall lung symptoms, monitoring may require hospitalization. You may require specific treatment in order to control pneumonitis. You may also be seen by a special doctor called a pulmonologist, who has special training to be an expert in how your lungs work.

Prolonged treatment with medicines that suppress inflammation, sometimes needed to manage the side effects of nivolumab treatment, may lower your body's ability to fight off certain infections (i.e., opportunistic infections). These infections may require treatment with antibiotic or antifungal medications and may be fatal.

<u>Rare but serious (<2%)</u>

- Low blood oxygen level
- Acute lung injury or failure
- Collection of fluid around the lungs
- Inflammation of the appendix
- Increase in inflammatory blood proteins (e.g., lipase)
- Adrenal gland abnormalities
- Pituitary gland inflammation
- Changes in vision (including decreased or blurry vision), inflammation of the eye, or bleeding into the eye

- Liver inflammation
- Acute kidney injury or failure
- Abnormal blood cell production
- Inflammation of the mouth and lining of the digestive tract
- Swelling of the face, arms, or legs
- Inflammation of the pancreas
- Back pain
- Autoimmune disorders, including Guillain-Barre syndrome (associated with progressive muscle weakness or paralysis)
- Chest discomfort
- Heart palpitations
- Inflammation of the heart or its lining
- Collection of fluid around the heart
- Increased blood sugar
- Dehydration
- Infections: including sepsis, lung infections, and skin infections.
- Decreased movement of the intestines
- Disorientation
- Swelling of the optic disc
- Inflammation of the optic nerve
- Inflammation or loss of the lining of the brain and spinal cord
- Drug reaction with rash, blood cell abnormalities, enlarged lymph nodes, and internal organ involvement (including liver, kidney, and lung); known as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)
- Myasthenia gravis, a nerve disease that may cause weakness of eye, face, breathing, and swallowing muscles. One death in a patient who received nivolumab combined with ipilimumab was considered due to myasthenia gravis and severe infection (sepsis).
- Abnormal brain function due to brain inflammation (encephalitis), potentially life-threatening or fatal.
- Toxic epidermal necrolysis, a potentially fatal disease characterized by blistering and peeling of the top layer of skin resembling a severe burn, has occurred in patients who received nivolumab treatment.
- Rhabdomyolysis (muscle fiber released into the blood stream which could damage your kidney) and polymyositis (chronic muscle inflammation with muscle weakness) has been reported in one patient.

Risks and side effects related to the **gemcitabine** include those which are:

Likely (≥ 20%)

- Leukopenia/Neutropenia (low white blood cell count) – a low white blood cell count makes it hard for you to fight infections Thrombocytopenia (low platelet count)– platelets are important in stopping bleeding. A low platelet count can increase the time to form a blood clot, causing you to bruise or bleed more easily
- Anemia (low hemoglobin, low hematocrit or low red blood cell count) Red blood cells carry oxygen and nutrients throughout the body. Symptoms that may be experienced as a result of low red blood cell counts may include feeling tired and weak, shortness of breath, increased heart rate, dizziness or lightheadedness, headache, chest pain and pale skin
- Nausea – feeling sick to your stomach
- Vomiting – throwing up

- Rash , with or without itching, usually over the legs (but can be on other parts of your body)
- Diarrhea – increased frequency of bowel movements with loose watery stools
- Elevated liver enzymes – liver enzymes are proteins made by the liver that are measured in the blood, with a blood draw. Liver enzymes indicate how well your liver is functioning. Elevated liver enzymes may cause no symptoms, however higher liver enzyme levels may cause you to feel overly tired or weak, you may bruise or bleed more easily, and you may experience abdominal pain or have a yellowing of the skin or eyes
- Hyperbilirubinemia (elevated bilirubin levels in the blood) – bilirubin is a chemical that is released when red blood cells are broken down. Bilirubin is used by the liver to make bile. Symptoms of elevated bilirubin levels include a yellowing of the skin, eyes and mucous membranes
- Flu-like symptoms including fever, chills, muscle aches and pain
- Fever
- Pain, including bone pain
- Fluid retention, swelling of the hands, legs or feet
- Shortness of breath
- Proteinuria – abnormal levels of protein in the urine, which may indicate kidney damage
- Small amounts of blood in your urine (may indicate a problem with your kidneys)
- Constipation – difficulty having a bowel movement

Less Likely (5-19%)

- Hair loss
- Mucositis/stomatitis – sores in the lining of your mouth and/or throat that can be painful and make it hard to swallow
- Peripheral neuropathy – numbness and tingling in hands and feet
- Somnolence – feeling sleepy
- Radiation recall – redness, burning, shedding or peeling of the skin where you have had radiation
- Elevation in serum creatinine, an enzyme in your blood, which may or may not indicate damage to your kidneys

Rare but serious (<5%)

- Congestive heart failure – a decrease in the heart's strength and ability to pump blood to the rest of the body
- Heart attack – symptoms may include chest pain/tightness, shortness of breath, nausea, sweating and dizziness
- Changes in heart rhythm
- Stroke – symptoms may include a sudden numbness or weakness of the face, arms or legs (usually on one side of the body), dizziness, severe headache, confusion, difficulty speaking or understanding, trouble walking and a sudden loss of balance
- Kidney failure
- Liver failure
- Pneumonitis – inflammation of the lungs which may cause shortness of breath, chest pain and cough
- Reversible Posterior Leukoencephlopathy Syndrome (RPLS) – a neurological disorder which can present with a headache, confusion, seizures, vision changes

- Tissue Necrosis – the death of body tissue which occurs when there is not enough blood flowing to the tissue. Necrosis is not reversible. When large areas of tissue die due to a lack of blood supply, the condition is called gangrene.
- Capillary leak syndrome – a condition in which fluid and proteins leak out of tiny blood vessels and flow into other tissues, resulting in dangerously low blood pressure

Radiation Risk for Diagnostic Imaging

- It is unlikely that there will be any harmful effects from the radiation exposure you will receive from participating in this study.
- At high levels of exposure, scientists agree that radiation can cause cancer.
- At low exposure levels most scientists agree that the risk, if any, is very low. You will have low levels of radiation exposure with diagnostic imaging procedures.
- Risks from exposure to radiation may accumulate over a lifetime.

Blood Draw Risks

- Fainting
- Bleeding
- Bruising at the place on your arm where the blood was drawn or needle inserted
- Pain
- Swelling
- Infection (rare)

Biopsy Risks

- Bleeding
- Pain
- Infection, which can be life-threatening or fatal in rare cases

Reproductive Risks

- The drugs in this study may affect a baby, before or after the baby is born.
- You should not become pregnant or father a baby while on this research study because the drugs you take could possibly hurt an unborn baby.
- If you are pregnant now or if you are breast-feeding now, you may not take part in this research study.
- If you become pregnant while you are on the research study, you may not continue to take part in the research study. Your pregnancy will be reported to Bristol Myers Squibb, the manufacturer of nivolumab, and followed for outcome.

For women who can become pregnant:

- You should not become pregnant while you are in this study and up to 23 weeks from the last dose of nivolumab.
- You should not breast-feed your baby while taking drugs for this research study and up to 23 weeks from the last dose of nivolumab.
- You will have a pregnancy test within first 24 hours of your first dose of nivolumab and then once every cycle during the course of this study.
- If you become pregnant, suspect pregnancy or if you missed your period or it is late, or if you have a change in your usual menstrual cycle (e.g., heavier bleeding during your period or bleeding between periods), you should immediately contact your study doctor.

- You are expected to use one of the highly effective methods of contraception listed below.
    - ✓ Progestogen only hormonal contraception associated with inhibition of ovulation
    - ✓ Hormonal methods of contraception including oral contraceptive pills (combination of estrogen and progesterone), vaginal ring, injectables, or implants
    - ✓ Intrauterine devices (IUDs) (hormonal or non-hormonal)
    - ✓ Intrauterine Hormone-releasing System (IUS)
    - ✓ Bilateral tubal ligation
    - ✓ Vasectomy
    - ✓ Complete abstinence (complete avoidance of heterosexual intercourse)

For men:

- You should not make a woman pregnant while you are in this study and up to 31 weeks after the last dose of nivolumab.
- If you are with female partners who are women of child bearing potential, you are expected to use condoms as the method of contraception
- You should immediately contact your study doctor if your female partner becomes pregnant while you are in this study. If your partner does become pregnant, it will be reported to Bristol Myers Squibb and followed for outcome.

For women and men:

- Check with the study doctor about birth control methods and how long to use them. Some methods might not be approved for use in this study.

Are there benefits to taking part in the study?

Taking part in this study may or may not make your health better. While doctors hope that nivolumab in combination with gemcitabine will be more useful against cancer compared to the usual treatment, there is no proof of this yet. We do know that the information from this study will help doctors learn more about the combination therapy as a treatment for non-small cell lung cancer. This information could help future cancer patients.

What other choices do you have if you do not take part in this research study?

Your other choices may include:

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting no treatment
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Talk to your doctor about your choices before you decide if you will take part in this study.

Will your medical information be kept private?

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.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- Fox Chase Cancer Center and affiliated Joint Centers, The Institutional Review Boards of The Fox Chase Cancer Center and Temple University, Temple University, Temple University Health system, Inc., and its affiliates or subsidiaries and other authorized representatives of these organizations.
- Bristol Myers Squib
- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people

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.

You will be given a separate form to review regarding the steps we will take to guard your privacy as part of your participation in the research study. By signing that additional authorization, you will be providing your consent to use and disclose information described in that form connected with your participation in this research study.

What are the costs?

You and/or your health plan/insurance company will need to pay for some or all of the costs of treating your cancer in this study. Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

The pharmaceutical company Bristol Myers Squib will supply nivolumab at no charge while you take part in this study. Bristol Myers Squib does not cover the cost of getting nivolumab ready and giving it to you, so you or your insurance company may have to pay for this.

Even though it probably won't happen, it is possible that the manufacturer may not continue to provide nivolumab for some reason. If this would occur, other possible options are:

- You might be able to get nivolumab from the manufacturer or your pharmacy but you or your insurance company may have to pay for it.
- If there is no nivolumab is available at all, no one will be able to get more and the study would close.

If a problem with getting nivolumab occurs, your study doctor will talk to you about these options.

You will be administered gemcitabine in addition to nivolumab. Gemcitabine is commercially available and will be billed to you in the same way you are usually billed for medicines.

If your insurance will not pay for medicines you may need to help with side effects, you may have to pay for them.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://cancer.gov/clinicaltrials/understanding/insurance-coverage . You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

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

Will you be compensated?

You will not be paid for taking part in this study.

What if you are injured while taking part in this research study?

If you are injured as a result of your participation in this research study, seek immediate medical care. Temple University Health System or its subsidiaries will treat the injury, though there is no commitment to provide monetary compensation or free medical care. Other financial compensation (such as lost wages or pain and suffering) for such injuries is not available.

What are your rights if you take part in this research study?

Taking part in this research study is your choice. You may choose either to take part or not to take part in the research study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

New findings

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

Who can answer your questions about the research study?

Important Contact Numbers	
If you are enrolled at the Fox Chase location (333 Cottman Ave)	
If you have questions about:	Please Call:
This study, including if you get sick or hurt	Dr. Martin Edelman at 215-728-4300
If you have a concern or complaint	Risk Management Department at 215-728-2591
Your rights as a research participant on this study	FCCC Institutional Review Board at 215-214-3754
Your bills or health insurance coverage	Clinical Trial Financial Counselor at 215-214-3768

Where can you get more information?

You may call the National Cancer Institute's Cancer Information Service at:

1-800-4-CANCER (1-800-422-6237)

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

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

By signing below, you tell us that you have gotten all of the information you need; that you have received clear answers to your questions, and that you agree to take part in the research study. You will receive a copy of this form. You may also request a copy of the research plan.

Signature of Participant	**Print Name of Participant**	**Date**

By signing this form the Physician obtaining consent indicates that the research participant has been fully informed of all aspects of the research study.

Signature of Physician Obtaining Consent	**Print Name of Physician Obtaining Consent**	**Date**

By signing this form the person obtaining consent indicates that the research participant has been fully informed of all aspects of the research study.

Signature of Person Obtaining Consent	**Print Name of Person Obtaining Consent**	**Date**

Signature of Legally Authorized Representative (LAR)	**Date**

Print Name of LAR	**Relationship of LAR to Participant**

(Indicate why the LAR is authorized to act as a surrogate health care decision-maker under the Commonwealth of Pennsylvania)

Informed Consent Document for Use of Tissue/blood for Research

Please note: This section of the informed consent form is about additional research studies that are being done with people who are taking part in the main study. You may take part in these additional studies if you want to. You can still be a part of the main study even if you say 'no' to taking part in any of these additional studies.

You can say "yes" or "no" to each of the following studies. Please mark your choice for each study.

About Using Tissue/blood for Research

Tissue requirement for participating in this study is optional if you already have a biomarker testing done otherwise it is required for study entry.

We would like to keep some of the tissue that is left over for future research. The tissue for future research is not mandatory. In addition we would also like to collect some blood for future research that is optional as well (1.5 tablespoon, every other cycle starting from cycle 1). If you agree, this tissue and blood will be kept and may be used in research to learn more about cancer and other diseases. If you would like to read more about how tissue/ blood is used for research, you can visit the National Cancer Institutes' website at http://www.cancer.gov/clinicaltrials/learningabout/providingtissue

The research that may be done with your tissue / blood is not designed specifically to help you. It might help people who have cancer and other diseases in the future.

Reports about research done with your tissue/blood will not be given to you or your doctor. These reports will not be put in your health record. The research will not have an effect on your care.

Things to Think About

The choice to let us keep the left over tissue and blood for future research is up to you. No matter what you decide to do, it will not affect your care.

If you decide now that your tissue / blood can be kept for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use your tissue/blood. Then any tissue/blood that remains will no longer be used for research.

In the future, people who do research may need to know more about your health. While we may give them reports about your health, we will not give them your name, address, phone number, or any other information that will let the researchers know who you are.

Sometimes tissue/blood is used for genetic research (about diseases that are passed on in families). Even if your tissue is used for this kind of research, the results will not be put in your health records.

Your tissue/blood will be used only for research and will not be sold. The research done with your tissue may help to develop new products in the future.

Benefits

The benefits of research using tissue include learning more about what causes cancer and other diseases, how to prevent them, and how to treat them.

Risks

The greatest risk to you is the release of information from your health records. We will do our best to make sure that your personal information will be kept private. The chance that this information will be given to someone else is very small.

Making Your Choice

Please read each sentence below and think about your choice. After reading each sentence, circle "Yes" or "No." If you have any questions, please talk to your doctor or nurse, or call our research review board at 215-214-3754.

No matter what you decide to do, it will not affect your care.

1. My tissue/blood may be kept for use in research to learn about, prevent, or treat cancer.

   YES NO

2. My tissue/blood may be kept for use in research to learn about, prevent or treat other health problems (for example: diabetes, Alzheimer's disease, or heart disease).

   YES NO

3. Someone may contact me in the future to ask me to take part in more research.

   YES NO

By signing below, you tell us that you have gotten all of the information you need; that you have received clear answers to your questions, and that you agree to take part in the research study. You will receive a copy of this form. You may also request a copy of the research plan.

Signature of Participant	**Print Name of Participant**	**Date**

By signing this form the Physician obtaining consent indicates that the research participant has been fully informed of all aspects of the research study.

Signature of Physician Obtaining Consent	**Print Name of Physician Obtaining Consent**	**Date**

By signing this form the person obtaining consent indicates that the research participant has been fully informed of all aspects of the research study.

Signature of Person Obtaining Consent	**Print Name of Person Obtaining Consent**	**Date**

Signature of Legally Authorized Representative (LAR)	**Date**

Print Name of LAR	**Relationship of LAR to Participant**

(Indicate why the LAR is authorized to act as a surrogate health care decision-maker under the Commonwealth of Pennsylvania)

FOX CHASE CANCER CENTER
TEMPLE HEALTH

FOX CHASE CANCER CENTER
AT TEMPLE UNIVERSITY HOSPITAL
All hospital services provided by Temple University Hospital

Authorization (Permission) to Use or Disclose (Release) Protected Health Information (PHI) for Research

IRB# and Protocol ID: 17-1050:TH-113
Study Title: **Depletion of Myeloid Derived Suppressor Cells to Enhance anti-PD-1 Therapy**

Principal Investigator: Martin J. Edelman, MD
Sponsor: Martin J. Edelman, MD at Fox Chase Cancer Center

1. What is the purpose of this form?

This form is required by the Health Insurance Portability and Accountability Act of 1996. Specifically the privacy regulation (HIPAA) permits the research investigators listed above to use and disclose health information about you for the research study identified above which has been approved by the Fox Chase Cancer Center Institutional Review Board.
The sponsor is an organization/person that does research to learn about the causes of cancer, and how to prevent and treat cancer. Researchers would like to use your protected health information for research. The elements of protected health information as defined by HIPAA are:

Data Elements for Protected Health Information (PHI)

- Names
- All geographic subdivisions smaller than a state (except for the first 3 digits of the zip code in some cases)
- All elements of dates (except year) for dates directly related to an individual (e.g., birth date, admission date, discharge date, date of death) and all ages over age 89 and dates indicative of that age
- Telephone numbers
- Fax numbers
- E-mail addresses
- Social security numbers
- Medical record numbers
- Health plan beneficiary numbers
- Account numbers
- Certificate/license numbers
- Vehicle identifiers and serial numbers, including license plate numbers
- Device identifiers and serial numbers
- Web Universal Resource Locators (URL)
- Internet Protocol (IP) addresses
- Biometric identifiers, including finger and voice prints
- Full face photos and any comparable images
- Any other unique identifying number, characteristic, or code

2. What protected health information do the researchers want to use?
The researchers want to copy and use the portions of your medical record that they will need for their research. If you enter a research study, medical information that will be used and/or released may include the following:

- The history and diagnosis of your disease
- Specific information about the treatments you received, including previous treatment(s) you may have had
- Information about other medical conditions that may affect your treatment
- Medical data, including laboratory test results, tumor measurements, CT scans, MRIs, x-rays, and pathology results
- Long-term information about your general health status and the status of your disease
- Data that may be related to tissue, urine and/or blood samples that may be collected from you

You may request a blank copy of the data forms from the study doctor or his/her research staff to learn what information will be shared.

3. Why do the researchers want my protected health information?
Fox Chase Cancer Center will collect your protected health information and share it with the sponsor, as applicable, if you enter a research study. The centers will use your information in their cancer research study.

4. Who will be able to use my protected health information?
Fox Chase Cancer Center, Temple University, Temple University Health System affiliates, and Temple University Clinical Faculty Practice Plan will use your health information for research. As part of this research, they may give your information to the following groups taking part in the research. Fox Chase Cancer Center and Temple University may also permit these groups to come in to review your original records that are kept by Fox Chase Cancer Center so that they can monitor their research study.

- Bristol Myers Squib
- The Fox Chase Cancer Center IRB
- Public Health agencies and other government agencies (including non-U.S.) as authorized or required by law
- Other people or organizations assisting with research efforts of the sponsor
- Central laboratories, central review centers, and central reviewers. The central laboratories and review agencies may also give your health information to those groups listed above

5. How will information about me be kept private?
The sponsor will keep all patient information private to the extent possible, even though the sponsor is not required to follow the federal privacy laws. Only researchers working with the sponsor will have access to your information. The sponsor will not release personal health information about you to others except as authorized or required by law. However, once your information is given to other organizations that are not required to follow federal privacy laws, we cannot assure that the information will remain protected. However, the laws of the Commonwealth of Pennsylvania or your state of residence may provide further privacy protection.

6. What happens if I do not sign this permission form?
If you do not sign this permission form, you will not be able to take part in the research study for which you are being considered.

7. If I sign this form, will I automatically be entered into the research study?

No, you cannot be entered into any research study without further discussion and separate consent. After discussion, you may decide to take part in the research study. At that time, you will be asked to sign a specific research consent form.

Treatment by your physician will not be affected by whether you provide authorization for the requested use or disclosure except if your treatment is related to research.

8. What happens if I want to withdraw my permission?

You can change your mind at any time and withdraw your permission to allow your protected health information to be used in the research. If this happens, you must withdraw your permission in writing. Beginning on the date you withdraw your permission, no new protected health information will be used for research. However, researchers may continue to use the protected health information that was provided before you withdrew your permission. If you sign this form and enter the research study, but later change your mind and withdraw your permission, you will be removed from the research study at that time.

To withdraw your permission, please contact the person below. He will make sure your written request to withdraw your permission is processed correctly.

Contact Name:	Martin J Edelman
Contact Address:	333 Cottman Avenue Philadelphia, PA 19111
Contact Phone and FAX:	215-728-4300 and 215-728-3639

9. How long will this permission last?

If you agree by signing this form that researchers can use your protected health information, this permission has no expiration date. However, as stated above, you can change your mind and withdraw your permission at any time.

10. What are my rights regarding access to my personal health information?

You have the right to refuse to sign this permission form. You have the right to review and/or copy records of your protected health information kept by Fox Chase Cancer Center and Temple University affiliates. However, while the research study is in progress, you may not be able to access your protected health information in order to preserve the integrity of the research. You will be able to access this information when the study is completed. You do not have the right to review and/or copy records kept by the sponsor or other researchers associated with the research study.

****

Signatures
I agree that my protected health information may be used for the research purposes described in this form.

_____	_____	_____
Signature of Participant	**Print Name of Participant**	**Date**

By signing this form the physician indicates that the research participant has been fully informed of all aspects of the research study.

_____	_____	_____
Signature of Physician	**Print Name of Physician**	**Date**

_____	_____	_____
Signature of Person Obtaining Consent	**Print Name of Person Obtaining Consent**	**Date**

_____	_____
Signature of Legally Authorized Representative (LAR)	**Date**

_____	_____
Print Name of LAR	**Relationship of LAR to Participant**

(Indicate why the LAR is authorized to act as a surrogate health care decision-maker under the Commonwealth of Pennsylvania)
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