PENN MEDICINE RESEARCH SUBJECT COMBINED INFORMED CONSENT FORM AND HIPAA AUTHORIZATION

Protocol Title:	PARPVAX: A Phase 1B/2, open label study of Niraparib plus either Ipilimumab or Nivolumab in patients with advanced Pancreatic Cancer whose disease has not progressed on platinum- based therapy
Funding Supporters:	Bristol-Myers Squibb and TESARO, Inc. a GlaxoSmithKline (GSK) Company
Regulatory Sponsor	University of Pennsylvania
Principal Investigator:	Kim Reiss Binder, MD Abramson Cancer Center of the University of Pennsylvania Philadelphia, PA 19104 215-360-0735
Sub-investigators:	Mark O'Hara, MD; Ursina Teitelbaum, MD; Robert Vonderheide, MD; Charles Schneider, MD; Thomas Karasic, MD, Jennifer Eads, MD
Emergency Contact:	24 Hour Emergency – Call 215-662-4000 Ask for Oncologist On-Call

Summary

You are being invited to participate in a research study. Your participation is voluntary and you should only participate if you completely understand what the study requires and what the risks of participation are. You should ask the study team any questions you have before agreeing to join the study. If you have any questions about your rights as a human research participant at any time before, during or after participation, please contact the Institutional Review Board (IRB) at (215) 898-2614 for assistance.
You are being invited to participate in a research study because you have pancreatic cancer. This research study is designed to learn more about the safety and effectiveness of drugs niraparib with either ipilimumab or nivolumab given to individuals who have been diagnosed with pancreatic cancer . You may or may not receive direct medical benefit from participating in this study. The hope is that this study treatment may provide a new treatment option for patients with pancreatic cancer, however, such a benefit cannot be guaranteed.

If you agree to join the study, you will be asked to complete the following research procedures: research blood tests and tumor biopsy. Additional procedures that are consistent with your standard of care treatment will also be performed.

Your participation will last up to until your disease progresses or you experience side effects that require treatment be stopped. Even after you discontinue study treatment, you will be contacted 30 days, 90 or 100 days and then annually by a study team representative who will ask questions about your health.
The following are some of the most commonly observed side effects: with Niraparib decreased blood cells such as white blood cells, red blood cells, and platelets; with Nivolumab fatigue, rash, diarrhea, and with Ipilimumab increased liver enzymes. . There is always the possibility that unknown risks and side effects may occur. These may be mild or very serious, and in some cases, may be very serious, long-lasting, or may never go away. There may also be a risk of death.

Other treatment options may be available to you. These could include treatment of your symptoms, without any effect on your disease, and/or treatment with currently approved drugs for pancreatic cancer .

Your study doctor or regular doctor can discuss alternate treatments available for your condition, and any known risks related to these treatments.

The possible benefit to you with the study drug has not been determined in clinical trials. You may also decide to forego further treatment. Please note that there are other factors to consider before agreeing to participate such as additional procedures, use of your personal information, costs, and other possible risks not discussed here. You are free to decline or stop participation at any time during or after the initial consenting process.

Why am I being asked to volunteer?

You are being asked to participate in this research study because you have been diagnosed with advanced Pancreatic Cancer. Your participation is voluntary, which means you can choose whether or not you want to participate. If you elect to participate in this study, you will not receive the standard of care for your diagnosis. Standard of care treatments are approved by the FDA have known benefits for your condition, therefore if you are interested in standard of care treatment you should first discuss your options with your primary care physician. If you choose not to participate, your clinical care will not be affected. Before agreeing to participate in this research study, it is important that you read the following explanation of the proposed procedures and how long you will be in the study. This document describes the purpose, procedures, benefits, risks, discomforts and precautions of the study. It also describes the alternative procedures that are available to you and your right to withdraw from the study at any time.

Please take time to read the following information carefully. You may wish to discuss it with your family, friends, and your personal doctor (i.e., your family doctor or primary care doctor). If you have any questions, you may ask your study doctor and/or the research team for more information. Take time to decide whether or not you wish to take part. If you decide to participate, you will be asked to sign this form. If you decide to participate, you can change your mind at any time and withdraw from the study without giving a reason.

What is the purpose of this research study? What does this study involve?

The main purpose of this study is to look at the effectiveness, safety, and antitumor activity (preventing growth of the tumor) of the drugs niraparib with either ipilimumab or nivolumab on you and on your pancreatic cancer.

The United States Food and Drug Administration (US FDA) is an authority that regulates new medicines. The study drugs niraparib, ipilimumab and nivolumab are approved by the US FDA to treat certain types of cancer. However, the use of niraparib, ipilimumab and nivolumab in this study is investigational because these drugs are not approved to treat advanced pancreatic adenocarcinoma and they have not been used in combination. However, all three drugs have been used and approved in other cancers. Additionally, PARP inhibitors such as niraparib have been combined with immune checkpoint medications such as ipilimumab and nivolumab in laboratory cancer models, and have been shown to be effective in killing cancer cells when used together.

This study will involve two different treatment arms. In Arm A patients will receive niraparib plus nivolumab. In Arm B patients will receive niraparib plus ipilimumab. Patients will be randomized to one of the two treatment arms.

Who is sponsoring this study?

Penn Medicine is the Regulatory Sponsor and Dr. Kim Reiss Binder, the Clinical and Scientific Expert and Penn Principal Investigator, is responsible for the design, conduct and regulatory oversight of the study. TESARO Inc. (now owned by GSK) is the manufacturer of the study drug, niraparib, and will be providing the drug during this research study. Bristol Myers Squibb (BMS) is the manufacturer of the study drugs,

nivolumab and ipilimumab and will be providing these drugs during this research study. TESARO Inc. and BMS are not the sponsor of this trial; however, Dr. Kim Reiss Binder and Penn Medicine will receive payments to cover some of the research costs such as the collecting/reporting study information associated with the conduct of the study.

How long will I be in the study?

You may continue to participate on this study until your disease gets worse, you experience unacceptable side effects, and/or your physician no longer believes the therapy is of benefit to you (whichever occurs first).

Once you stop the study drug treatments, there will be an End of Treatment visit and a 30-days follow-up visit. After your 30-day follow-up visit you will be followed for safety up to 100 days. Then the study team will contact you annually by telephone, email, monitor your medical records, or at your clinical visits to ask you questions about your health. You may stop your participation in the study at any time.

What am I being asked to do?

If you meet all of the criteria for being in the study, you will be registered to participate. The study procedures are outlined below; however due to the COVID-19 Pandemic some procedures may be modified to protect your safety and these modifications will be discussed with you during this consent process.

Screening Procedures: These procedures are done to evaluate your cancer, overall health, and eligibility. If you have had some of these tests/procedures recently, they may not need to be repeated. These tests and procedures need to be done within 28 days before you receive your first dose of study drug, unless otherwise indicated.

- A review of your history to include: a review of your medical and cancer history to make sure you do not have any conditions that could interfere with your taking part in this study (this will include the review of results from genetic testing you have already had); you will be asked how you are feeling; a review of the medications you are taking, including all prescription medications and all non-prescription medications (such as vitamins, herbal supplements, aspirin, etc.); a review of your social history (such as if you are a smoker and how much alcohol you may drink); and a review of any significant medical or surgical procedures you have had.
- Your demographic information will be captured which include your gender, age, race, and ethnicity
- A complete physical examination including height and weight.
- An assessment of how your disease affects your daily living abilities (called Performance Status).
- Measurement of your vital signs (blood pressure, pulse, and temperature).
- Approximately 2 teaspoons of blood will be drawn to determine your eligibility. The routine tests being done to determine your eligibility and for safety purposes will test your blood cell counts (number of each type of blood cell), blood chemistry levels (to test your kidney and liver function and the minerals in your body), test for thyroid gland problems and a serum pregnancy test for women of child bearing potential. If the pregnancy test comes back positive you will not be allowed to participate in this study.
- Blood sample (about 1 teaspoon of blood) for HIV viral status testing to check if you have these viruses. This is to ensure you are healthy enough to enter the study.
    - This would not typically be done as a part of your standard of care treatment.
- Radiology tests - to assess your disease. These assessments may include a CT (computed tomography) scan, MRI (magnetic resonance imaging) scan, PET/CT (positron emission tomography/computed tomography) scan, and/or a chest x-ray.

- You must agree not to donate blood during your participation and for 90 days after the last dose of treatment.

Once you have passed the screening, but before you begin receiving study drug, the following may be performed:

- If you have stored tumor tissue available from a previous biopsy, this will be documented and we will collect some of the stored tumor tissue for research testing prior to conclusion of the study.
    - This would not typically be done as a part of your standard of care treatment.
- If you have a tumor that can easily be reached, you will be asked to allow your doctor to complete a tumor biopsy and remove a small amount of tumor. This is a required part of this study (is not optional) if the biopsy is feasible. Providing this type of tumor sample is essential in helping us learn about your specific disease and how we and help other patients like you.
    - This would not typically be done as a part of your standard of care treatment.

Procedures associated with the administration of the study drug(s)
When all of the above tests/procedures have been completed, if you have been found to be eligible to enter this study, and you agree to participate, you will randomized to treatment Arm A or Arm B and be scheduled to receive the study drugs.

Study drugs will be given over many cycles. A cycle is the time between the start of 1 round of treatment until the start of the next round. In this study, Arm A with Nivolumab plus Niraparib treatment cycle is 28 days and Arm B with Ipilimumab plus Niraparib is 21 days. Cycles will continue until your cancer gets worse, you experience unacceptable side effects, your doctor no longer believes the therapy is in your best interest, or you no longer want to participate in the study.

In this study a process called randomization (like flipping a coin) will be used to determine who will receive Niraparib plus nivolumab OR Niraparib plus ipilimumab. Your chances are 50/50 of receiving nivolumab or ipilimumab.

Your doctor and the study team will inform you if you will receive Niraparib plus nivolumab OR Niraparib plus ipilimumab. Nivolumab and ipilimumab will be administered during your scheduled visit and all patients will be given a diary to document that the study medication, niraparib, will be taken at home between visits. You will be asked to bring this completed diary and your remaining study drug and/or empty pill bottles to each study visit. When you return this study drug bottles and diary, the study team will review everything to make sure you are taking the drug appropriately and completing this diary as requested.

If you are randomized to receive niraparib plus nivolumab (Arm A), treatment is as follows beginning on Day 1 of each 28 day cycle:

- Niraparib- two 100 mg pills by mouth (oral) daily
- Nivolumab- 30 minutes (IV, into a vein) every 4 weeks (Day 1 of every cycle)

If you are randomized to receive niraparib plus ipilimumab (Arm B), treatment is as follows beginning on Day 1 of each 21 day cycle:

- Niraparib- two 100 mg pills by mouth (oral) daily
- Ipilimumab 30 minute (IV, into a vein) infusion on day 1 of the first 4 cycles. Niraparib will continue after you have stopped ipilimumab.

Study Tests/Procedures
These exams, tests, and procedures are being done to evaluate your health and response to the study drugs. At each of these study visits you will be asked how you are feeling, if you have had any side

effects, if you may be pregnant, if you have had any medical procedures, and about any medications you are taking. It is important you check with your study doctor before starting any new medications. Taking other drugs (including alcohol, over-the-counter medications, herbal preparations, illegal drugs, or nutritional supplements) may cause additional side effects or even life-threatening reactions when combined with the drugs being used in this study. If you experience side effects, changes in your health and/or changes in medications, please contact your study doctor or a study team member.

You will have the following tests, procedures, and assessments done at the time points below:

Arm A Schedule		
Procedure/Study Day	**Day 1 of each cycle[7]**	**Weekly**
Physical Exam, Weight	X	
Performance Status Evaluation	X	
Vital Signs	X	
Blood Pressure and heart rate monitoring	X	X[5]
Safety Blood Tests - about 2 teaspoons will be collected[4]	X	
Research Blood Tests - about 5 tablespoons will be collected[1]	X[6]	
Pregnancy Blood Test	X	
Review of Adverse Events	X	
Review of Concomitant Medications and Procedures	X	
Disease Assessment/Tumor Scans[2]	X	
Tumor Biopsy [1,3]	X	

1. This procedure would not typically be done as a part of standard of care treatment. We will collect research blood tests every other cycle or every 8 weeks.
2. Tumor scans to be performed within 7 days prior to start of every 2nd cycle (every odd numbered cycle), or approximately every 8 weeks
3. A tumor biopsy will be performed at Cycle 2 day 1 unless it is deemed unsafe by the study doctor or if there appears to be no evidence of disease (complete remission)
4. For safety purposes you will have a blood test for blood cell counts (number of each type of blood cell) once a week during the first 4 weeks on treatment
5. You will be required to take your blood pressure and heart rate once every week during the first 2 months you are taking Niraparib and record this information on your study drug diary. This will also be taken at the start of each cycle while you are participating.
6. An additional research blood draw may be performed on day 8 of cycle 1
7. Patients on Arm A who are (1) clinically stable (as per the investigator) following 11 full cycles of treatment and (2) are no longer receiving nivolumab may go twelve weeks (i.e. three cycles) between clinical assessments and disease assessment imaging. For these patients, three cycles of niraparib may be dispensed at one time. However, all safety blood work must still be collected at D1 (+/- 3 days) of each cycle and will be reviewed by the research team.

ARM B Schedule		
Procedure/Study Day	**Day 1 of each cycle[7]**	**Weekly**
Physical Exam, Weight	X	
Performance Status Evaluation	X	
Vital Signs	X	
Blood Pressure and heart rate monitoring	X	X[5]
Safety Blood Tests – about 2 teaspoons will be collected[4]	X	
Research Blood Tests - about 5 tablespoons will be collected[1]	X[6]	
Pregnancy Blood Test	X	
Review of Adverse Events	X	
Review of Concomitant Medications and Procedures	X	
Disease Assessment/Tumor Scans[2]	X	
Tumor Biopsy[1,3]	X	

1. This procedure would not typically be done as a part of standard of care treatment. We will collect research blood tests every other cycle or every 8 weeks.
2. Tumor scans to be performed within 7 days prior to start of every 3rd cycle, or approximately every 9 weeks
3. A tumor biopsy will be performed at within 7 days of Cycle 2 day 1 unless it is deemed unsafe by the study doctor or if there appears to be no evidence of disease (complete remission)
4. For safety purposes you will have a blood test for blood cell counts (number of each type of blood cell) once a week during the first 4 weeks on treatment
5. You will be required to take your blood pressure and heart rate once every week during the first 2 months you are taking Niraparib and record this information on your study drug diary. This will also be taken at the start of each cycle while you are participating.
6. An additional research blood draw may be performed on day 8 of cycle 1
7. Patients on Arm B who are stable (as per the investigator) following 17 full cycles of treatment may go twelve weeks (i.e. four cycles) between clinical assessments and disease assessment imaging. For these patients, four cycles of niraparib may be dispensed at one time. However, all safety blood work must still be collected at D1 (+/- 3 days) of each cycle and will be reviewed by the research team.

End of Study Visit:

The following procedures will be performed for all patients as soon as possible after the last dose of study treatment:

- A complete physical examination including weight
- You will be asked how you are feeling, if you have had any side effects, if you may be pregnant, if you have had any medical procedures, and about any medications you are taking.
- An assessment of how your disease affects your daily living abilities (called Performance Status)
- Measurement of your vital signs (blood pressure, pulse, and temperature)
- Approximately 6 tbsp. of blood will be drawn
    - The routine tests being done will test your blood cell counts (number of each type of blood cell), blood chemistry levels (to test your kidney and liver function and the minerals in your blood), and markers of cancer in your blood (CA19-9).

  - The research tests being done to detect potential markers of pancreas cancer in the blood such as tumor cells and tumor genetic material (DNA). This would not typically be done as a part of your standard of care treatment.
  - If you are a woman of child-bearing potential, a pregnancy blood test will also be done. This would not typically be done as a part of your standard of care treatment.
- Radiology tests to assess your disease. These assessments may include a CT scan, MRI scan, PET/CT scan, and/or a chest x-ray
- You will have a review of all niraparib tablets you brought back to the study center and a review of your completed study drug dosing diary

Post-Study Procedures:
You will be asked to come in again 30 days after you have finished study treatment for a review of your general health and to see whether anything new has happened to you since your last study visit, including any side effects you may be experiencing.

- Report any changes in health (including any side effects)
- Radiology tests to assess your disease. These assessments may include a CT scan, MRI scan, PET/CT scan, and/or a chest x-ray (if not already done for End of Treatment visit)

After this visit, the study staff will continue to follow up with you for up to 100 days for safety. Then annually by telephone, email, medical record review, or at a clinic visit to see how you are doing.

What are the possible risks or discomforts?

As with all research studies, the study treatment and study procedures may involve unknown risks. Any medication can have temporary or permanent side effects that may or may not be expected. While on the study, you are at risk for the following side effects. Some of these side effects may be potentially serious or life-threatening, and may include death. You should discuss these with the study doctor. There also may be other side effects that are not known and other very rare side effects that are known but not included in this list. If you experience side effects from the study drug(s), your study doctor may delay or skip a dose of the study drug, or ask you to stop taking study drug. If you are told to stop taking one of the study medications, you may still continue to receive therapy of the other study medication. Your doctors may also give you other drugs to help lessen these side effects. Many side effects go away shortly after the study drug is stopped, but in some cases side effects can be serious, long lasting or permanent.

As there is no experience using niraparib in combination with nivolumab and ipilimumab in pancreatic cancer, it is not yet clear how they will work together. This means that it is possible that the study drug may change how well the routine care drugs work in treating your disease (i.e. may make it more or less effective).

Niraparib
The treatment with niraparib could result in side effects. The frequencies below are based on niraparib clinical trials.

Niraparib has moderate influence on the ability to drive or use machines. Patients who take niraparib may experience weakness, fatigue, difficulty concentrating and dizziness. Patients who experience these symptoms should observe caution when driving or using machines.

Known side effects of niraparib are listed below::

Very Common occurrence (may affect more than 1 in 10 people)

- Decrease in blood cells (red blood cells) that carry oxygen; this may make you feel tired or short of breath (anemia)
- Decrease in blood cells (platelets) that help stop bleeding; this may increase your risk of bleeding (thrombocytopenia)
- Decrease in neutrophils, one of several types of white blood cells that fight infection; this may decrease your ability to fight infections (neutropenia)
- Decrease in the number of white blood cells (leukopenia) that fight infection
- Increased blood pressure (hypertension)
- Noticeably rapid, strong, or irregular heartbeat (palpitations)
- Infrequent hard stools (constipation)
- Feeling sick to your stomach (nausea)
- Vomiting
- Feeling not hungry; decreased appetite
- Sleeplessness, trouble sleeping (insomnia)
- Headache
- Feeling tired, lack of energy (fatigue)
- Shortness of breath (dyspnea)
- Runny or stuffy nose (nasopharyngitis)
- Cough
- Feeling abnormal physical weakness or lack of energy (asthenia)
- Dizziness
- Joint pain (arthralgia)
- Back pain
- Stomach pain (abdominal pain)
- Indigestion (dyspepsia)
- Frequent watery stools (diarrhea)
- Painful and frequent urination (urinary tract infection)

Common occurrence (may affect up to 1 in 10 people):

- An abnormally rapid heart rate (tachycardia)
- Infection due to low white blood cell counts (neutropenic infection)
- Low blood cell counts due to a problem in the bone marrow or blood cancer starting from the bone marrow (Myelodysplastic Syndrome [MDS]/Acute Myeloid Leukemia [AML])
- An irritation or infection in the tubes that carry air in and out of the lungs, that causes a cough (bronchitis)
- Swelling of lower legs and feet (peripheral edema)
- Muscle pain (myalgia)
- Rash
- Decrease in weight
- Feelings of sadness, depressed (depression)
- Feelings of worry, nervousness or unease (anxiety)
- Impaired concentration, understanding, memory, and thinking (cognitive impairment)
- Inflammation of the eye (conjunctivitis)

- Nose bleed (epistaxis)
- Sore, red mouth (stomatitis)
- Swelling or irritation of the lining of the mouth, throat, esophagus, stomach or intestines (mucosal inflammation/mucositis)
- Abnormal taste in mouth (dysgeusia)
- Dry mouth
- Increased sensitivity of the skin to sunlight (photosensitivity)
- Decrease in potassium in the blood (hypokalaemia)
- Increased level of creatinine in your blood (blood creatinine increase), which may be a sign of kidney damage
- Increased levels of substances in the blood produced by the liver, which may be a sign of liver injury (aspartate aminotransferase [AST] increased, alanine aminotransferase [ALT] increased, gamma-glutamyl transferase [GGT] increased)
- Other abnormal labs (alkaline phosphatase [ALP] increased)
- Allergic reaction (hypersensitivity, including anaphylaxis)

Uncommon Occurrence (may affect up to 1 in 100 people):

- Fever with low white blood cell count (febrile neutropenia)
- Severe life-threatening infection due to low white cell counts (associated with low blood pressure and possible organ failure (for example, heart, kidney and/or liver) (neutropenic sepsis)
- Decrease in number of all types of blood cells (pancytopenia)
- Confusion (confusional state/disorientation)
- Seeing or hearing things that are not likely there (hallucination)
- Inflammation of the lungs which can cause shortness of breath and difficulty breathing (non-infectious pneumonitis)

Rare Occurrence (may affect up to 1 in 1000 people):

- Severe increase in blood pressure (hypertensive crisis)
- A brain condition with symptoms including seizures, headache, confusion, and changes in vision (posterior reversible encephalopathy syndrome [PRES])

Side Effects Requiring Immediate Medical Attention:
The side effects listed below require **IMMEDIATE MEDICAL ATTENTION OR ADVICE**. **Call the study doctor right away if you have any of these side effects:**

- Allergic reactions can be life-threatening. Symptoms may include difficulty breathing, shortness of breath, low blood pressure (feeling lightheaded, dizziness), tingling around the mouth, rash.
- Low platelet counts may increase your risk of bleeding and bruising. Bleeding may require urgent medical attention, including a transfusion (receiving blood or blood products by vein).
- Low red blood cell counts may make you feel tired or short of breath and symptoms may require a blood transfusion.
- Low neutrophil counts may be associated with infection, sometimes severe and life-threatening (neutropenic infection, neutropenic sepsis):
    - Symptoms of severe life-threatening infection may include:
        - Fever, feeling of low blood pressure (lightheadedness, dizziness), decreased urination, rapid pulse, rapid breathing or shortness of breath

- Decrease in the number of all types of blood cells (pancytopenia)
- Low blood cell counts due to a problem in the bone marrow or blood cancer starting from the bone marrow (MDS or AML). MDS/AML, including fatal cases, have been reported with use of niraparib. If you experience prolonged haematological toxicities, contact your study doctor for haematologist evaluation.
- High blood pressure (hypertension) including severe increase in blood pressure (hypertensive crisis) has been reported with the use of niraparib. If you have pre-existing hypertension, the physician will determine if your blood pressure is adequately controlled before starting niraparib treatment.
    - Symptoms of a severe increase in blood pressure may include:
        - Blurry vision, headache, nausea, vomiting, confusion, passing out, seizures, weakness or numbness on one side of body or in one arm or leg and/or difficulty talking (symptoms of a stroke), trouble breathing, chest pain, pain in the upper or lower back, urine that is brown or bloody
- Posterior Reversible Encephalopathy Syndrome (PRES), a rare neurological side effect has been reported with niraparib treatment.
    - If you have headache, vision changes, confusion or seizure with or without high blood pressure, please contact your doctor.

Class Effects:

Class effects are potential risks that are associated with a particular group of drugs. Niraparib belongs to the group known as poly (ADP-ribose) polymerase inhibitors (PARP) inhibitors. These class effects are potential risks for the group of drugs, but have not yet been identified as side effects for niraparib

Secondary Primary Malignancy:

- PARP inhibitors may also cause a new primary cancer (that is, a cancer other than the one for which you have been treated). In 2 studies comparing niraparib to placebo (sugar pill), new primary cancers were observed in a small number of patients who took niraparib or placebo.

Safe Handling:
Niraparib may have adverse effects on an unborn baby. Wash your hands after handling the Study Drug. If a caregiver is giving the Study Drug to you, he or she should wear disposable gloves. Notify your Study Doctor if it appears that the Study Drug is damaged or defective in any way.

Nivolumab
Nivolumab may cause one or more of the side effects listed below. This information is based on data from cancer subjects in other clinical trials with nivolumab. In addition, there may be side effects that are not yet known that may occur. You should tell your doctor or nurse right away about any possible side effects you experienced.

The most common side effects of Nivolumab are: [greater than or equal to 10%]

- Fatigue
- Rash
- Itching
- Diarrhea

Common side effects of Nivolumab include: [greater than or equal to 1% and less than 10%]

- Nausea

- Abdominal Pain
- Dry skin
- Redness of the skin
- Decreased appetite
- Fever
- Increased blood sugar
- Inflammation of the mouth and lining of the digestive tract
- Bowel inflammation
- Liver function blood test abnormalities
- Loss of color (pigment) from areas of skin
- Dry mouth
- Vomiting
- Thyroid gland abnormalities
- Blood chemistry abnormalities, including low blood phosphate, magnesium, and potassium levels.
- High blood uric acid level
- Lung inflammation (pneumonitis - see details below)
- Cough
- Dizziness
- Headache
- Chills
- Muscle soreness, weakness, stiffness spasms or paralysis
- Musculoskeletal pain
- Swelling of the face, arms, or legs
- Tingling, burning, weakness or numbness in arms, legs, hands and feet
- Shortness of breath
- Allergic reaction during or between study drug infusions
- Constipation

<u>Uncommon side effects [Less than 1%]</u>

- Joint pain or stiffness
- Adrenal gland abnormalities
- Inflammation of the pancreas
- Lung infection
- Dehydration
- High or low blood pressure
- Pituitary gland inflammation
- Abnormal taste
- Increased sensitivity of skin to sunlight
- Difficulty swallowing
- Double vision
- Diabetes
- Hives
- Dry eyes
- Hair loss

- Heart rate increased
- Heart rhythm abnormal
- inflammation of the eye
- Inflammation of the kidney
- Inflammation of the stomach
- Inflammation of the thyroid gland
- Liver inflammation
- Muscle inflammation
- Pemphigoid: blistering of the skin or mouth caused by the immune system attacking healthy tissue.
- Pituitary gland function decreased
- Psoriasis: characterized by patches of abnormal, scaly skin
- Renal (kidney) failure or kidney injury
- Respiratory failure
- Upper respiratory tract infection
- Vision Blurred

Rare but potentially serious side effects of Nivolumab include: [less than 0.1%]

- Collection of fluid around the lungs
- Anaphylactic Reaction (severe allergic reaction). Severe allergic reactions can be life threatening
- Cranial nerve disorder
- Damage to the protective covering to the nerves in the brain and spinal cord
- Drug induced liver injury
- Diabetes complications resulting in excess blood acids
- Disease caused by the body's immune system attacking healthy organs
- Inflammation of the blood vessels
- Inflammation of the brain, potentially life-threating or fatal
- Lung Infiltrates, association with infection or inflammation
- Inflammation of the appendix
- Increase in inflammatory blood proteins (e.g., lipase)
- Polymyalgia rheumatic an inflammatory disorder causing muscle pain and stiffness
- Abnormal blood cell production
- Back pain
- Autoimmune disorders, including Guillain-Barre syndrome (associated with progressive muscle weakness or paralysis)
- Inflammation of the heart or its lining, potentially life-threating or fatal
- Collection of fluid around the heart
- Stevens Johnson syndrome: inflammatory disorder of skin and mucous membranes, resulting in blistering and shedding of skin
- Syndrome associated with fever, white blood cell activation and abnormal function (including destruction of other blood cells by certain white blood cells), low blood cell counts, rash, and enlargement of the spleen
- Histiocytic necrotizing lymphadenitis or Kikuchi lymphadenitis: disorder of the lymph nodes which causes the lymph nodes to become enlarged, inflamed and painful, commonly affecting lymph nodes of the neck and possibly associated with fever or muscle and joint pains.

- Rosacea: acne-like skin condition resulting in redness of face
- Rupture of the intestine/hole in the intestine
- Sarcoidosis, a disease involving abnormal collections of inflammatory cells (granulomas) in organs such as lungs, skin, and lymph nodes
- 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.
- Vogt Koyanagi Harada syndrome; a disease that affects the pigmented tissue; this may affect the eye leading to swelling, pain and/or blurred vision; the ear leading to hearing loss , ringing in the ears and /or the skin leading to loss of skin color

Lung Inflammation (pneumonitis):
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 AT ONCE 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.

Complications, including fatal events, have occurred in patients who received allogeneic hematopoietic stem cell transplantation (HSCT) before or after nivolumab.

Complications, including rejection, have also been reported in patients who have received an organ or tissue transplant. Treatment with nivolumab may increase the risk of rejection of the organ or tissue transplant. These complications could be serious and possibly even fatal.

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.

Ipilimumab

Some of the side effects of ipilimumab may not cause you any symptoms, including changes in your liver or kidney function, changes in your thyroid, pituitary or adrenal gland function, changes in your blood count or changes in your electrolytes (salt levels in the blood). These will be assessed by the physician with blood tests at every treatment visit.

COMMON, SOME MAY BE SERIOUS

In 100 people receiving ipilimumab more than 20 and up to 100 may have:

- Diarrhea
- Swelling and irritation of the colon (colitis)
- Increase in liver enzymes
- Fatigue
- Skin itchiness
- Skin rash
- Nausea
- Abdominal pain
- Decreased appetite
- Fever
- Vomiting
- Headache
- Constipation
- Adrenal gland abnormalities, which may make you feel tired or make your blood pressure go down
- Thyroid gland abnormalities, which may make you feel tired or cold

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving ipilimumab from 4 to 20 may have:

- Chills
- Weakness
- Muscle pain
- Redness of skin

RARE, AND SERIOUS

In 100 people receiving ipilimumab 3 or fewer may have:

- Decrease or total loss in hormones of the pituitary gland, which may make you feel tired

- Allergic reactions
- Irritation of the liver
- Irritation and swelling of the pituitary gland, which may give you a headache
- Decreased red blood cells, which may make you feel tired or dizzy
- Loss of color (pigment) from areas of skin
- Decreased or blurry vision, or inflammation of the eye
- Numbness or tingling in your fingers or toes
- Inflammation or loss of the lining of the brain or spinal cord which may make you feel confused or give you a headache
- Inflammation of the kidneys
- Joint pain
- Pneumonitis

Death resulting from side effects considered related to ipilimumab occurred in about 1% of patients treated with ipilimumab in earlier clinical trials. Severe infections including sepsis have also been reported in ipilimumab-treated subjects, some of which resulted in death.

Other Study Related Risks

Risks of Using Up Stored Tumor Tissue Samples

If it is available, stored tumor tissue may be collected. It is possible that this entire stored sample will be used for the purposes of this research study and therefore may not be available for future clinical assessments as part of your routine care.

Risks of Biopsy

A biopsy is an invasive test in which your cells and/or tissue are collected for examination. It involves the surgical removal of a small bit of tissue for examination. Your study doctor will explain this procedure to you in more detail, and you will be given a standard hospital consent form to sign detailing your specific type of biopsy prior to the procedure.

Likely risks:

- Pain
- Discomfort
- Soreness
- Minor bleeding
- Bruising

Less likely risks:

- Redness
- Swelling
- Bleeding
- Pneumothorax (collapsed lung)

Rare risks:

- Bleeding, life threatening hemorrhage
- Possible damage to adjacent organs
- Drainage from the biopsy site
- Abnormal wound healing

- Fever
- Infection
- Allergic reaction to the medication used to numb the skin over the biopsy site

Blood Samples:
There may be side effects of having blood drawn such as:

- Fainting
- Redness
- Pain
- Bruising
- Bleeding
- Infection
- Blood clots, which may cause inflammation, swelling and pain

If you feel faint tell the study staff right away.

Risks of IV
An IV line will be used to administer study drug through a vein in your arm. The use of an IV line may cause discomfort, irritation, mild bruising, bleeding, leakage of drug solution, and rarely infection, nausea, and lightheadedness.

Risks of Infusion-Related Reaction
Infusions of drugs can cause allergic reactions in people. Allergic reactions may include shortness of breath, itching, rash, low blood pressure, and fever during the infusion or shortly after. If you experience any of these symptoms, you should contact your doctor immediately. Sometimes these reactions can be serious and can result in death if not watched carefully. You will be watched by medical personnel for signs of allergic reactions, and you will be given medicine if you need it.

Nivolumab will be administered at a faster infusion rate. There is not an increased risk to patients associated with shortening the infusion time.

Risks of Radiology Tests
During your participation in this study, you may undergo routine radiology tests to assess your disease. These can include CT, MRI, x-ray or PET scans. Each of these procedures has risks associated with it, and you should talk to your study doctor or the person doing these procedures about the risks before they start.

- Radiation Exposure: This research study involves exposure to radiation from the CT scans, PET scans and x-rays. Therefore, you will receive a radiation dose. At doses much higher than you will receive, radiation is known to increase the risk of developing cancer after many years. At the doses you will receive, it is very likely that you will see no effects at all.
- CT Scans: A CT scan is an imaging method that uses x-rays to create cross-sectional pictures of the body. You will be asked to lie on a narrow table that slides into the center of the CT scanner. Depending on the study being done, you may need to lie on your stomach, back, or side. Once you are inside the scanner, the machine's x-ray beam rotates around you. It is important to remain still during the exam, because movement causes blurred images. You may be told to hold your breath for short periods of time. The scans take about 15 minutes or less to complete.
    - It is important to inform your study doctor if you have had an allergic reaction to IV contrast material in the past, or if you have an allergy to iodine. Most CT contrast reactions (approximately 95%) are mild to moderate in degree and most resolve themselves without

treatment. However, life-threatening reactions and fatalities, mostly of cardiovascular origin, have occurred. People with heart disease, kidney disease or allergies are more likely to have a more severe reaction to contrast agents. If you have a history of kidney disease, allergies or heart disease, please inform the study staff. Likely contrast reactions include feelings of overall warmth (especially in the bladder area after injection), a metallic taste during the injection, and warmth, burning sensation, or momentary pain during the contrast injection at the injection site. Less likely contrast reactions include nausea, vomiting, headache, hives, and itching. Rare but serious contrast reactions include faster than normal heart rate (tachycardia), high blood pressure (hypertension), low blood pressure (hypotension), heart attack, kidney failure, fluid in the lungs (pulmonary edema), serious allergic reaction, and death. There is also a risk that multiple needle sticks will be necessary to ensure proper intravenous line placement. There may be a small amount of pain or bruising with the placement of the intravenous catheter (IV) and a small risk of infection at the injection site.

- MRI: The known risks associated with an MRI are minimal. The procedure uses radio waves and a magnetic field to take pictures. The greatest risk of having an MRI is the chance of metal objects flying through the air toward the magnet and hitting you. To reduce this risk, all people involved with the study are instructed to remove all metal from their clothing and all metal objects from their pocket. You must tell your study doctor if you have any metal plates or clips in your body. No metal objects are allowed to be brought into the magnet room at any time. Metal objects inside your body can affect the test results and could lead to injury. Because the magnetic field of the MRI scanner attracts metal, these studies will not be performed on anyone with a pacemaker or any non-removable metallic foreign objects in their body. If you have any such object on your body, you will not receive the scan. You may feel claustrophobic (fear of being closed in) or anxious. You may experience some discomfort and fatigue from lying in a confined space. There are no known effects from exposure to the magnetic fields. Multiple needle-sticks may be necessary if a vein cannot be properly accessed and this will be carried out upon your permission. It is possible that during the course of the research study, the research staff may notice an unexpected finding(s). Should this occur, the finding(s) will be considered by the appropriate personnel and the PI will inform you if necessary. These possible finding(s) may or may not be significant and may lead to anxiety about your condition and to further work-up by your physician.
- PET: A PET scan is a type of imaging test that helps doctors see how the organs and tissues inside the body are actually functioning. The test involves injecting a very small dose of a radioactive chemical, or radiotracer, into a vein. Although a radiotracer chemical is used in this test, the amount of radiation exposure is low. The dose of tracer used is so small that it does not affect the normal processes of the body. You may experience discomfort related to lying still for a prolonged period of time.

What about pregnancy and breastfeeding?

Reproductive Risks:
Study drugs may have adverse effects on an unborn baby. Study participants of reproductive potential must adhere to contraception (methods or ways to prevent pregnancy) requirements.

Effects of niraparib on fertility are unknown at this time. Animal studies in a drug similar to niraparib have been shown to cause a decrease in the number of cells that produce eggs in women's ovaries (reproductive organs).

Animal studies have shown that niraparib can cause a reversible decrease in sperm count. If you agree to participate in this study, you are expected to inform your female sexual partner(s) that you are participating in a clinical research study of an investigational drug, and that the effects of the drug on human sperm, an unborn baby and on a pregnant woman are unknown. You are also expected to provide your female sexual partner(s) with the information on the acceptable birth control methods described by your Study

Doctor and to provide her with contact information for the Study Doctor for any additional questions. If your female partner becomes pregnant while you are participating in this study or within 90 days after your last dose of Study Drug, tell your Study Doctor right away as the Study Doctor is required to follow up and document the course and the outcome of all pregnancies. The Study Doctor may seek the pregnant woman's permission to review her medical records and the infant's medical records up to delivery, if applicable. The Study Doctor will share the information about your pregnant partner and the baby with the Sponsor to help understand the effects, if any, that the Study Drug may have on the pregnancy and/or the baby.

Female Participants

You should not become pregnant while on this study and for 6 months after your last dose of study drug because the study drugs could have a negative effect on an unborn baby. In addition, you should not breastfeed while on this study as these drugs may also affect a breast-feeding child. People who are pregnant or breast-feeding (including expressing breastmilk for bottle feeding or storage) are not allowed to participate in this study. If you become pregnant, you will no longer be able to participate in this study.

If you are able to have children, you must agree to use two medically accepted forms of birth control including condoms, diaphragms, cervical cap, an intra-uterine device (IUD), intrauterine hormone-releasing system (IUS), surgical sterility (tubal ligation or a partner that has undergone a vasectomy), or oral, injectable, or implantable contraceptives, OR you must agree to completely abstain from intercourse during participation in this study and for 6 months after your last dose of study drugs. Abstinence at certain times of the cycle only, such as during the days of ovulation, after ovulation and withdrawal are not acceptable methods of birth control. Your study doctor must approve your form of birth control. Ask your study doctor about the contraceptive methods that are available and which might be the best for you.

Even when you use an approved contraceptive method, there is always a small risk that you could still become pregnant. If you do become pregnant during the course of this study, or up to 6 months after your last dose of study drug, you must discontinue study treatment, tell the investigator immediately, and consult an obstetrician or maternal-fetal specialist. If you become pregnant while on this study, we will ask permission to collect information about your pregnancy.

- Tell the study doctor if you are pregnant. If you get pregnant during the study, you will not receive any more niraparib, but you may remain in the study for follow-up. You must not breastfeed an infant (or store breastmilk for use) while taking the Study Drug and for 30 days after receiving final dose of Study Drug. We will follow-up until the delivery of the baby.

Male Participants

To participate in the study, male study participants must adhere to contraception (methods or ways to prevent pregnancy) requirements.

You should not father a child or donate sperm while on this study and for 90 days after your last dose of study drug, because the drug involved could have a negative effect on an unborn baby. If your spouse or partner has the potential to become pregnant, you and your partner must use two medically accepted forms of birth control including condoms, diaphragms, cervical cap, an intra-uterine device (IUD), intrauterine hormone-releasing system (IUS), surgical sterility (tubal ligation or a partner that has undergone a vasectomy), or oral, injectable, or implantable contraceptives, OR you must agree to completely abstain from intercourse during participation in this study and for 90 days after your last dose of study drugs. Abstinence at certain times of the cycle only, such as during the days of ovulation, after ovulation and withdrawal are not acceptable methods of birth control. Your study doctor must approve your form of birth control. Ask your study doctor about the contraceptive methods that are available and which might be the best for you.

You should also inform your partner of the potential harm to an unborn child. She should know that if a pregnancy should occur during the course of this study, or up to 90 days after your last dose of study drug,

you will need to report it to the study doctor immediately, and she should promptly notify her doctor. The study doctor will also ask to follow-up on the pregnancy.

Genetic Research Risks:
As part of this research study, the study team may perform genetic testing on your tumor and/or blood samples. These are experimental tests, not approved by the FDA, and will have no impact on your study participation. Results will not appear in your medical record and your doctor will not be notified directly. New health information about inherited traits that might affect you or your blood relatives could be found during the research study. Even though your genes are unique, you share some of the same genes with your blood relatives. Although we are not able to know all of the risks from taking part in research on inherited traits, we believe the risks to you and your family are very low, because your samples will be coded.

Very rarely health or genetic information could be misused by employers, insurance companies, and others. For example, life insurance companies may charge a higher rate based on this information. The chance that your information could be misused is very small. We have many protections in place to lower this risk. Your privacy will be protected to the fullest extent possible.

A new federal law called the Genetic Information Non-Discrimination Act, or GINA is in effect. This law helps to lower the risk of health insurance or employment discrimination. The law does not include other types of misuse by life insurance or long term care insurance. To learn more about the GINA Law, please check the Internet or ask the study staff.

What happens if we find a gene that might predispose you to getting cancer?

The genetic testing done as a part of this study is purely experimental. The results of these tests will not be included in your medical record. If during this experimental testing we identify a mutation in a gene that we think might predispose you to getting cancer, we will notify you of this finding. If you would be interested at that time in having clinical genetic counseling and confirmatory testing done, we can offer those services to you. Only the results of any clinical genetic testing you might choose to have done would be made a part of your medical record. A separate consent form that you will be given specifically for clinical genetic testing will explain in detail that testing and how the results may be used.

In the event we identify a gene mutation and you cannot be contacted, you may indicate the name and contact information of the person we may release this information to at the end of this form.

What if new information becomes available about the study?

During the course of this study, we may find more information that could be important to you (such as new information about how the drug works or newly discovered side effects). If we discover new information about the study that could affect your decision to stay in the study, you will be notified in a timely manner. You will be able to ask questions about this new information and can discuss it with your family, friends, or doctor.

What are the possible benefits of the study?

Taking part in this study may or may not make your health better. However, while you may not benefit personally, the knowledge learned from your participation in this research study may benefit other patients in the future. It is possible that your disease and/or health may worsen as a result of participating in this study.

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

Your participation in this study is entirely voluntary. Other possible options include:

- Getting treatment or care for your cancer without being in a study.

- Taking part in another study.
- Not receiving treatment at this time.
- 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 I be paid for being in this study?

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

Will I have to pay for anything?

The Drug manufacturers TESARO/GSK and BMS will supply the study drugs at no charge while you take part in this study. The cost of drug administration may be the responsibility of you and/or your insurance provider. Upon the trial's completion, Bristol-Myers Squibb Company will not continue to supply study drug to subjects/investigators. Your doctor is responsible to ensure that you receive appropriate standard of care or other appropriate treatment to treat your condition.

You will be responsible for any deductibles or applicable co-pays for the standard tests, exams or procedures that would be done for your routine clinical care, such as office visits, scans and blood work. You and/or your insurance provider will be responsible for standard tests, exams or procedures that would be done even if you were not in this study. Please talk to your doctor and study team about putting you in touch with a financial counselor to determine exactly what the deductible and co-pay will be for you; this is highly variable depending on your type of insurance. There will be no charge to you for those laboratory tests and other procedures that are being done specifically for the purposes of this research study.

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

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.

What happens if I am injured or hurt during the study?

If you have a medical emergency during your participation on this study, you should go to the nearest emergency room. You should contact the Principal Investigator or Emergency contact listed on page one of this form. You may also contact your own doctor, or seek treatment outside of Penn Medicine. Be sure to tell the doctor or his/her staff that you are in a research study being conducted at the University of Pennsylvania. Ask them to call the telephone numbers on the first page of this consent form for further instructions or information about your care.

Penn Medicine will offer you the care needed to treat side effects and/or injuries that occur while you are taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them. There are no plans for Penn Medicine, Bristol Myers Squibb, or TESARO/GSK to pay you or give you other compensation for the injury.

Financial compensation for such things as traveling, parking, lost wages, disability or discomfort due to injury is not routinely available.

You will not lose any of your legal rights when you sign this form.

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

You may continue to participate on this study until your disease gets worse, you experience unacceptable side effects, and/or your physician no longer believes the therapy is of benefit to you, whichever occurs first. The doctor may stop you from taking part in this study at any time if he/she believes that it is in your best interest, if you do not follow the study rules, or if the study is stopped. If new information becomes available that might affect your choice to stay in the study; your study doctor will notify you as soon as possible.

You may stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to your doctor first. You can also choose to leave the study at any time without giving a reason. It is important to tell the doctor if you are thinking about stopping so any risks for the treatments that you received can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you. Leaving the study will not affect your future medical care.

The doctor may stop you from taking part in this study at any time if he/she believes that it is in your best interest, if you do not follow the study rules, or if the study is stopped. If new information becomes available that might affect your choice to stay in the study, your study doctor will notify you as soon as possible.

This study may also be stopped at any time by your study doctor, the study Sponsor, or the Food and Drug Administration (FDA) without your consent because:

- The Principal Investigator or the sponsor feels that it is in your best interest to discontinue the study. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions, or you become pregnant
- The Sponsor, the study Principal Investigator, or the Food and Drug Administration (FDA) has decided to stop the study due to new information regarding side effects.
- It is determined that you are no longer benefiting from the study therapy
- For any other reason that is not known at this time

If you are removed from the research study, your study doctor will explain to you why you were removed. The study doctor and study team will help arrange for your continued care.

How will my personal information be protected during the study?

If you decide to participate in this study, the study doctor and staff will collect medical and personal information about you as part of completing the study. We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. This study is being overseen by the Food and Drug Administration (FDA); therefore, they may review your research records. Please refer to the information below which explains more specifically how your personal information will be protected. If you do not want to allow these uses, you should not participate in this study. Information identifying you will be kept confidential as described below.

While collected as part of this study by your study doctor and study team, identifying information (including your name, address, telephone number, medical record number, or any number/codes that will directly identify you) will be kept as confidential as possible and will not be routinely disclosed outside Penn Medicine. Personal health information that could be used to identify you will not be sent to drug Manufacturers, TESARO/GSK and BMS and/or their designated representatives.

You will be assigned a unique subject registration number upon enrollment. This number and your initials will be used to identify you throughout the course of this study so that your identity is protected. The key to this code (which links your name back to the personal health information collected during this study) will be stored in a secure area and only the Penn Medicine study team will have access to this code. However, some of the study data (e.g. date of birth) could be used in combination with other information, in order to identify you. If you have questions about the specific information that will be released, you should ask your study doctor.

If you test positive for HIV, by law we have to report the positive test results to the City of Philadelphia Health Department and/or the PA Department of Health. Personal identifiers such as name, sex, date of birth, address, and phone number will be reported. For more information about the requirements reporting infectious diseases to the City of Philadelphia Health Department, please visit https://hip.phila.gov/ReportDisease. For more information about the requirements reporting infectious diseases to the PA Health Department, please visit http://www.health.pa.gov And type 'Reportable Diseases' into the site search bar.

Will information about this study be available to the public?

A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by US Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

What may happen to my information and samples collected on this study?

Whole genome sequencing may be conducted on your samples. Whole genome sequencing involves analyzing your entire personal genetic code.

Future Use of Data and/or Specimens

Your identifiable information and samples will be stored for future research purposes. Future researchers may receive information that could identify you. This can be done without again seeking your consent in the future, as permitted by law. The future use of your information and samples only applies to the information and samples collected on this study.

The following identifiers will be retained with your information and samples: The information and samples will be labeled with your study ID. The study ID is linked back to your identifiable information (i.e. the master list).

Your information and samples may be stored and used for future research purposes for an indefinite amount of time.

There are no plans to tell you about any of the specific research that will be done. Possible future research may include additional studies that further characterize tumor and host factors that may influence response and resistance to treatment.

We may share your deidentified information and samples with other research, academic, and medical institutions, other researchers, drug and device companies, biotechnology companies and others. Samples are planned to be shared with BostonGene for analysis.

We will not follow up with you to tell you about the specific research that will be done. We will not give you any results from these future studies, but will give you results if a cancer pre-disposing gene mutation is identified. It is possible that you may have chosen not to participate in these future research studies, had you been approached for participation.

There is a risk of breach of confidentiality (unintentional release of your information). We will do our best to make sure that this doesn't happen. However, we cannot guarantee total privacy. We will protect your confidentiality during storage and sharing by not releasing identifiable information. Your information and samples will be labeled with a code that links you to the information (i.e. master list), but we will not share the master list.

You will likely not directly benefit from future research with your information and samples. Research with your identifiable information and samples may help others by improving our understanding of health and disease, improving health care and making safer or more effective medical therapies, and developing new scientific knowledge.

If you have questions about the storage of your information and samples, or have changed your mind, you can contact Dr. Reiss Binder at 215-360-0735. If you change your mind, you can ask to have the data collected about you removed or the samples destroyed. You can also ask us to remove information that identifies you from the data or samples. However, this may not be possible if your samples and data have already been shared.

Electronic Medical Record and Release of Study Related Information?

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

If you have never received care within Penn Medicine and are participating in a Penn Medicine research study that uses Penn Medicine healthcare related services, an EMR will be created for you for the purpose of maintaining any information produced from your participation in this research study. The creation of this EMR is required for your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have). If you have been a patient at Penn Medicine in the past, information from your research participation will be added to your existing medical record.

What may be placed in the EMR?

Information related to your participation in the research (e.g., laboratory tests, notes from your physician, imaging studies, and clinical procedures, etc.) will be placed in your EMR maintained by Penn Medicine. Once placed in your EMR, your information may be accessible to appropriate Penn Medicine workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by Penn Medicine to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc.).
Penn Medicine also participates in automated information sharing through Health Information Exchanges (HIEs). HIEs securely share parts of your electronic health record, including research information, with other healthcare organizations involved in your care. This information is shared to improve the quality, safety and efficiency of your healthcare. To request that your health information not be shared through HIEs, please call 215-662-4484.

Will I, as a subject, have access to research related information within the EMR?

Please note the following about diagnostic test and/or imaging results:

- The 21st Century Cures Act requires healthcare institutions to allow patients increased access to their electronic medical record. As part of your participation in this research, you will have access to

research related information within your EMR through Penn Medicine's patient portal – called MyPennMedicine (MPM).

- Results that may be placed in the medical record: Results from testing conducted in a laboratory or center that is part of Penn Medicine (i.e., the results would have been placed in the medical record, regardless of research participation). Results placed in the medical record are part of the designated record set and you have a right to review these results per HIPAA regulations.
- Results that may not be placed in the medical record: Results from biospecimen testing conducted in a laboratory that is not part of Penn Medicine and/or results from testing conducted in a non-certified laboratory (i.e., the results would not have been placed in the medical record as part of clinical care).

Will I receive the results of research testing?

Clinically relevant research results will be disclosed to you; this will be done in the context of discussion with your study doctor and/or clinical treatment team. Results from clinical testing done as part of this research will be placed in your medical record. Results placed in the medical record and will be available to you per HIPAA regulations, as noted above.

What information about me may be collected, used or shared with others?

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

- Name, address, telephone number, gender, date of birth, email address
- The history and diagnosis of your disease
- Specific information about the therapy you received, including previous treatment(s) you may have had
- Information about other medical conditions that may affect your care
- Medical data including laboratory test results, health status, CTs, x-rays, MRIs, PETs, pathology results, etc.
- Information on side effects (adverse events) you may experience, and how these were treated
- Long-term information about your general health status and the status of your disease. This may include information from other health care providers.
- Data that may be related to tissue samples that may be collected from you
- Numbers or codes that will identify you, such as your medical record number
- Information related to study visits and other tests/procedures performed while you are participating on this study.

Why is my personal health information being used?

Your personal contact information is important for the research team to contact you during the study. For this study we may need to contact you via email to provide you information about scheduling, appointments, notes or to send you information about your participation in the study. Email communications are often not secure and may be seen by others as a result. By signing below, you accept this risk. If you wish for us to use a different means to communicate with you during the course of this study, please discuss this with the research team and alternative methods can be arranged.

Your personal health information and results of tests and procedures are being collected as part of this research study, and will be used to conduct and oversee this research study, and to help guide your medical care.

Where may my information be stored?

Information related to your participation in clinical research will be contained in a clinical trial management system (CTMS). A clinical trial management system (CTMS) is used to register your information as a participant in a study. This allows for your research data to be entered and stored for the purposes of study operational and financial applications and other activities required as part of the conduct of the research. Once placed in the CTMS your information may be accessible to other authorized personnel at Penn Medicine that support research operations. Your information may be held in other research databases

You will be assigned a unique subject registration number upon enrollment. This number and your initials will be used to identify you throughout the course of this study so that your identity is protected. The key to this code (which links your name back to the personal health information collected during this study) will be stored in a secure area and only the Penn Medicine study team will have access to this code. However, some of the study data (e.g. date of birth) could be used in combination with other information, in order to identify you. If you have questions about the specific information that will be released, you should ask your study doctor.

Who can see or use my information?

Which personnel may use or disclose my personal health information?

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

- The Principal Investigator and the Investigator's study team
- Authorized members of Penn Medicine and Penn Medicine support offices, who may need to access your information in the performance of their duties (for example: for research oversight and monitoring, to provide care as part of this study or as part of your routine care, to manage accounting or billing matters, etc.). This includes members of the Institutional Review Board (IRB), an Ethics Committee at Penn Medicine who are responsible for reviewing and overseeing research studies to ensure that they are safe and being well managed.
- Other research personnel with access to the databases for research and/or study coordination and as otherwise approved by the IRB

Who, outside of Penn Medicine, might receive my personal health information?

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

Your original medical records also may be reviewed by the sponsor of this study or its designated representatives, the Institutional Review Board overseeing this study, and any of the regulatory or safety oversight organizations outlined below. They may review these records for the purpose of checking data collected for the study, to make sure the study is being done properly, and to analyze the results of the study.

Individuals or organizations responsible for administering the study:

- Bristol-Myers Squibb and their designated representatives
- TESARO/GSK and their designated representatives
- Penn Medicine and Kim Reiss Binder, MD
- BostonGene

Regulatory and safety oversight organizations

- The U.S. Food and Drug Administration (FDA)
- Office for Human Research Protections (OHRP)
- Other regulatory agencies and/or their designated representatives, including international agencies
- Public Health agencies and other government agencies (including non-U.S.) as authorized or required by law

Once your personal health information is disclosed to others outside Penn Medicine, it may no longer be covered by United States federal privacy protection regulations.

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

How long may Penn Medicine be able to use or disclose my personal health information?

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

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

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

The data from this study may be published or used for teaching purposes, however you will not be personally identified in any publication. Your identity will remain confidential unless disclosure is required by law.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

Can I change my mind?
You have the right to withdraw your permission for the use of your personal health information, but if you do so, you must stop taking part in this study. You must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, your personal health information that was collected before we received your written request may still be used and disclosed, as necessary for the study. If you withdraw your permission to use your personal health information, you will also be withdrawn from the research study and no new information will be collected. However, even if you do withdraw your permission to use the data about you, we are required by the FDA and other national regulatory authorities to record anything that relates to the safety of the investigational drug under study.

Will I be able to access my research records?
You have the right to see and get a copy of your medical records kept by Penn Medicine. However, you will not be able to review or receive some of your records related to the study until after the entire study has been completed. When the study is over, you may write to the study doctor to ask to see or copy all of

your medical information that was collected during the study. You also have the right to say how your medical information may be used, and to have any incorrect data about yourself updated or corrected.

A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by US Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

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

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

If you have questions, concerns or complaints regarding your participation in this research study you should speak with the Principal Investigator listed on page one of this form. If you have any questions about your rights as a research subject, you may contact the Office of Regulatory Affairs at Penn Medicine with any questions, concerns or complaints by calling (215) 898-2614.

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

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, the study has been explained to you, your questions have been answered, you have had time to make your decision, and you have decided to volunteer to participate. You have been given the names of study staff that you can contact if you need assistance or if you have any additional questions or concerns. You agree to follow all of the instructions of your study doctor to the best of your ability, and report any changes in your health that may occur during the study.

Your signature also means that you are permitting Penn Medicine to use your personal health information collected about you for research purposes within our institution. You are also allowing Penn Medicine to disclose that personal health information to outside organizations or people involved with the operations of this study.

You agree that your primary care physician can be informed about your participation in this clinical trial.

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

1. I agree to the storage of my blood for use now and for future research:

Yes **No** **Initials: _____**

2. I agree to the storage of my tumor tissue for use now and for future research:

Yes **No** **Initials: _____**

If a cancer-predisposing gene mutation is identified and I am unable to be contacted, this information may be released to:

Name: _____

Phone Number: _____

Email Address: _____

☐ Check here and initial if you do not wish this information to be released **Initials: _____**

_____	_____	_____
Name of Subject (Print)	Signature of Subject	Date
_____	_____	_____
Name of Person Obtaining Authorization (Print)	Signature of Person Obtaining Authorization	Date

For subjects unable to give authorization, the authorization is given by the following authorized subject representative:

Name of Legally Authorized Subject Representative (Print)	Signature of Legally Authorized Subject Representative	Date

Provide a brief description of above person's authority to serve as the subject's authorized representative.