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Official Title:	A Phase II Study of Preoperative Pembrolizumab for Mismatch-Repair Deficient, Epstein-Barr Virus Positive and/or PD-L1 Positive Gastric Cancer followed by Chemotherapy and Chemoradiation with Pembrolizumab
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CONSENT TO TAKE PART IN A RESEARCH STUDY

TITLE OF STUDY: A Phase II Study of Preoperative Pembrolizumab for Mismatch-Repair Deficient, Epstein - Barr virus Positive and/or PD-L1 Positive Gastric Cancer followed by Chemotherapy and Chemoradiation with Pembrolizumab

PRINCIPAL INVESTIGATOR: Salma Jabbour, MD
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STUDY-RELATED PHONE NUMBER(S): 732-235-2465 (24 hours)

This consent form is part of an informed consent process for a research study and it will provide information that will help you to decide whether you wish to volunteer for this research study. It will help you to understand what the study is about and what will happen in the course of the study.

If you have questions at any time during the research study, you should feel free to ask them and should expect to be given answers that you completely understand.

The study doctor, Salma Jabbour, MD, or another member of the study team will also be asked to sign this informed consent. You will be given a copy of the signed consent form to keep.

You are not giving up any of your legal rights by volunteering for this research study or by signing this consent form.

Even after signing this consent form, you may withdraw from the study at any time.

Sponsor of the study
The Rutgers Cancer Institute is the sponsor of this study. Merck & Co., Inc will supply the study drug, Pembrolizumab (MK-3475) and is providing funding support.

Why is this study being done?
The standard treatment for your type of cancer is surgery to remove the tumor, followed by treatment with chemotherapy plus radiation therapy. Giving chemotherapy drugs and radiation therapy after surgery can reduce the risk of the cancer coming back in some patients. Researchers want to know if adding a drug, pembrolizumab, before surgery and again after surgery with chemotherapy and radiation therapy is better at keeping the cancer from coming back. This study is being done to test the good and bad effects of the study drug called pembrolizumab when given before surgery and again in combination with chemotherapy and radiation after surgery. The chemotherapy you will be receiving is capecitabine.

Pembrolizumab is a PD-1 inhibiting drug. Typically, the human body's immune system recognizes abnormal cells in the body and destroys them. Cancer cells frequently create proteins on the cell

surface (PD-L1) that act as signals to turn off this part of the immune system. Pembrolizumab is a drug that blocks (inhibits) this signal on the immune system's cells (PD-1) and allows the immune system to recognize these cancer cells as foreign.

Pembrolizumab is FDA approved to treat melanoma, Hodgkin's lymphoma, lung and head and neck cancers. The use of pembrolizumab in this study is investigational. "Investigational" means that this medication has not yet been approved by the FDA to treat the type of cancer you have.

The purpose of this study is to find out the effects (good or bad) of giving pembrolizumab before surgery and then again in combination with capecitabine and radiation therapy.

Why have you been asked to take part in this study?
You are being asked to take part in this study because you have gastric cancer and your treatment plan includes surgery followed by capecitabine and radiation therapy.

Who may take part in this study? And who may not?
You may take part in this study if you are 18 years of age or greater with gastric cancer. Additionally, you may take part in this study if:

- Your treatment plan includes surgery followed by capecitabine and radiation therapy
- Your cancer has Mismatch Repair Deficiency (failure to repair errors that occur during cell division), Epstein-Barr Virus positive (a virus in the herpes family) and/or Programmed Death Ligand 1 positive (a marker on tumors that helps tumors hide from the immune system)
- You have tumor available from a recent surgery or biopsy
- You have read and signed this Informed Consent Form

You may not take part in this study if:

- You have received prior treatment for gastric cancer
- You have cancer that has spread to other parts of the body
- You are unable to keep your doctor's appointments
- You are pregnant or breast feeding

How long will the study take and how many subjects will participate?
You will receive treatment for approximately 17 months, as long as your cancer does not come back and you are not experiencing severe side effects. After you have stopped receiving treatment on study, we will continue to follow up with you for the rest of your life.

A total of approximately 40 patients will take part in this study. You will be one of approximately 25-30 patients enrolled at the Rutgers Cancer Institute.

What will you be asked to do if you take part in this research study?
<u>Before you begin study treatment:</u>
You will have some exams, tests and procedures to find out if you can take part in this study. Most of the exams, tests, and procedures you will have are part of the usual approach for your cancer. However, your doctor will do some extra testing as part of the study. The testing that you will need to have if you take part in this study is discussed below. If some of these have been done recently they may not need to be repeated, this will be up to the study doctor.

- Your age and race/ethnicity will be recorded.

- You will be asked about your medical history and any medications you are currently taking, both prescription and over the counter.
- You will have a complete physical examination, with your physician or physician's assistant, including measurement of your vital signs (breathing rate, blood pressure, temperature, and heart rate), height, and weight.
- Evaluation of your ability to carry out daily activities.
- The following blood samples will be collected:
    - Approximately 2 teaspoons (10 mL) for routine testing, such as, a complete blood count, kidney and liver function tests to ensure that it is safe to administer any of the drugs included in this study
    - Approximately 1 teaspoon (5 mL) for blood clotting tests
    - Approximately 1 teaspoon (5 mL) for thyroid function testing
- Urinalysis (urine test)
- If you are a woman who could become pregnant (even if you had a tubal ligation), your doctor will perform a blood or urine pregnancy test. If you are pregnant, you cannot participate in this study.
- Imaging tests typically performed for cancer patients, including imaging of chest, abdomen and pelvis. Tests will include:
    - Computed tomography (CT), a scan that uses x-rays to look at one part of your body. It may be done with or without contrast. Contrast means that dye is injected into your vein to increase the differences between normal and abnormal tissue.
    - Positron emission tomogram (PET), uses computerized images to look at the activity of tumor cells in your entire body and that requires injection of a special marker into your vein, such as sugar (glucose) combined with a low-dose radioactive substance (a tracer). A camera records the tracer's signal as it travels through your body.
    - Laparoscopy, a surgical procedure in which a fiber-optic instrument is inserted through the abdominal wall to examine the cancer
    - Endoscopic ultrasound, a procedure using ultrasound (sound or other vibrations) to examine the walls of the upper and lower gastrointestinal tract and organs near it
- You will be asked to provide a sample of your tumor for research from a recent surgery or biopsy (within 10 weeks). If your tumor specimen is greater than 10 weeks old, you may still be able to take part in the study if the tumor is available and the sponsor gives permission.

  Your doctor will send the tumor sample to a central lab for testing of certain proteins and biomarkers (indicators of normal biological or disease processes) that may be involved in PD-1 activation or to understand the nature of your disease. These laboratory tests are new and under development. Any remaining slides after the testing is completed will be destroyed.

If you do not meet the eligibility requirements, you cannot take part in this study. The study doctor will inform you of other options that are available to you.

STUDY TREATMENT

If the tests, exams, procedures show that you can be in the study, you will be enrolled. All study participants will receive the following treatment (1 cycle = 21 days):

- 2 cycles of pembrolizumab, followed by a 2-6 week break
- Surgery, followed by a break of up to 56 days
- 1 cycle of capecitabine with pembrolizumab
- 2 cycles of capecitabine and radiation therapy with pembrolizumab, followed by a 2- 6 week break
- 2 cycles of capecitabine with pembrolizumab
- Maintenance pembrolizumab

Pembrolizumab: You will receive pembrolizumab by IV through a vein over 30 minutes Day 1 of every 21 day cycle.

Surgery: You will be scheduled for surgery to remove your cancer after 2 cycles of pembrolizumab.

Chemotherapy: You will receive capecitabine. Capecitabine is given in pill form, which you will take by mouth twice a day on Days 1 thru 14 of every 21 day cycle. The dose of capecitabine you take will depend on your height and weight, so your doctor will tell you how many pills you will take.

Radiation Therapy:
You will receive radiation therapy daily (Monday thru Friday) for 5-6 weeks (25 treatments total). Each treatment may take up to 15-30 minutes depending on the technique used.

Your doctor will decide what type of radiation therapy you will receive.

- 3-Dimensional conformal radiation therapy or intensity modulated radiation therapy (IMRT) is a form of radiation in which a number of x-ray beams are used to shape the radiation to the cancer and is designed to avoid important normal parts of your body.
- Image guided radiation therapy (IGRT) radiation is part of the routine radiation treatment that helps to align the radiation accurately to the tumor. Small adjustments in your radiation treatment are made each treatment day based on x-ray images taken right before each day's treatment to ensure that your radiation treatment is given as accurately as possible.

Before you begin radiation therapy, you will have imaging of the chest in order to design your radiation treatment. Doctors will use information gathered from these scans to plan the best way to deliver radiation to your tumor.

On the next page is a table of the treatment plan.

Cycle (1 cycle = 21 days)	Drug	Treatment Day
Cycles 1 –and2	Pembrolizumab	Day 1 of every 21 day cycle
2 – 6 week break		
Surgery		
Up to 56 day break after surgery		
Cycle 3	Pembrolizumab Capecitabine	Day 1 of every 21 day cycle Days 1 thru 14 twice a day of every 21 day cycle
Cycles 4 and 5	Pembrolizumab Capecitabine Radiation Therapy	Day 1 of every 21 day cycle Days 1 thru 14 twice a day of every 21 day cycle Monday thru Friday x 5 weeks
2 – 6 rest period		
Cycles 6 and 7	Pembrolizumab Capecitabine	Day 1 of every 21 day cycle Days 1 thru 14 twice a day of every 21 day cycle
Cycles 8 thru 18	Pembrolizumab	Day 1 of every 21 day cycle

While on study treatment:
During the treatment period, you will need the following examinations, tests, and procedures described below. Some of these exams, tests, and procedures are part of your regular medical care.

Day 1 of every 21 day cycle:

- You will be asked to report any symptoms and health problems you have and any new medications you have started.
- You will have a complete physical examination, with your physician or physician's assistant, including measurement of your vital signs (breathing rate, blood pressure, temperature, and heart rate), height, and weight.
- Evaluation of your ability to carry out daily activities.
- You will have blood tests:
    - Approximately 2 teaspoons (10 mL) for routine testing, such as, a complete blood count, kidney, and liver function tests.
    - Approximately 1 teaspoon (5 ml) for thyroid function
- Urinalysis (urine test)
- *Tumor Assessments:* You will have imaging after surgery and then every 3 months while receiving treatment to make sure your cancer has not come back.

After you have completed study treatment:

Your doctor will stop study treatment if any of the following occur:

- Your cancer comes back
- You develop unacceptable side effects
- You become pregnant or are unwilling to use appropriate birth control techniques
- The study doctor determines that it is not in your best interest to continue the study treatment
- You have completed study treatment as planned
- New information becomes available
- The study is stopped by the Sponsor, Merck & Co., Inc., or the IRB or the FDA
- You choose to stop study treatment

After all study treatment has stopped, your doctor will ask you to return to the clinic for an end of treatment visit:

- You will be asked to report any symptoms and health problems you have and any new medications you have started.
- You will have a complete physical examination, with your physician or physician's assistant, including measurement of your vital signs (breathing rate, blood pressure, temperature, and heart rate), height, and weight.
- Evaluation of your ability to carry out daily activities.

Follow-Up

If you have any ongoing side effects at the time you complete the study or your doctor discontinues you from the study, the study doctor will continue to follow/monitor your condition until the side effect resolves or becomes stable.

You will return for follow up visits 30 days after the last dose of study drug, then every 3 months for the first year, then every 4 months for year 2, and then every 6 months for years 3 -5. The following assessments will be done at these visits:

- You will be asked to report any symptoms and health problems you have and any new medications you have started.
- You will have a complete physical examination, with your physician or physician's assistant, including measurement of your vital signs (breathing rate, blood pressure, temperature, and heart rate), height, and weight.
- Evaluation of your ability to carry out daily activities.
- You will have blood tests (at the 30 day post-treatment visit):
    - Approximately 2 teaspoons (10 mL) for routine testing, such as, a complete blood count, kidney, and liver function tests.
    - Approximately 1 teaspoon (5 ml) for thyroid function
- Urinalysis (urine test)
- Tumor Assessments by scan

If your cancer returns or you withdraw from the study treatment but not from study follow-up, the study staff will contact you approximately every 12 weeks after your last visit to check on your health status. If they are not able to reach you, they may use a public information source (like county records) to obtain information about your survival status only, which will be reported as part of the data for the study.

Specimens for Research
Researchers will be collecting specimens (tumor and blood) to see how the immune system responds to the treatment. Tumor sample will be taken prior to treatment and at the time of surgery. In addition, blood samples will be collected for research at various time points. The research that will be done with your tissue and blood is not designed specifically to help you. It might help people who have cancer and other diseases in the future.
Specimens will be collected at the following time points:

Fresh tumor specimens will be collected at:

1) Baseline, (either from a previous biopsy, if available; or a fresh sample if the doctor requires another biopsy for medical reasons),
2) at surgery.

Approximately 8 teaspoons (40 mL) of blood will be collected on:

1) Prior to Cycle 1
2) surgery,
3) prior to Cycle 3,
4) prior to Cycle 4,
5) prior to Cycle 8,
6) and at treatment discontinuation.

Second Course Treatment:
You may be eligible for up to one year of additional pembrolizumab therapy if the cancer comes back after stopping pembrolizumab. Your study doctor will determine if you meet the study criteria to be eligible for the Second Course Treatment. If you are eligible, you will restart treatment at the dose and dose frequency received upon initial treatment with pembrolizumab.

What are the risks and/or discomforts you might experience if you take part in this study?
You may have side effects from the drugs or procedures used in this study, and they will vary from person to person. Study doctors will carefully watch everyone taking part in the study for any side effects. However, the study doctors and the study funders do not know all the side effects that may happen, and unknown side effects that could occur. The study doctors may give you medicine to help lessen the side effects. In some cases, side effects can be serious, long lasting, and/or may never go away. There also is a rare risk of death. You should talk to your study doctor about any side effects that you have while taking part in the study.

If you experience any severe side effect, you should:

- Seek professional medical help immediately
- Call your study doctor
- If necessary, go to the nearest emergency room

Possible Side Effects of Capecitabine Likely:

- Nausea (feeling as if you are about to throw up)
- Diarrhea (frequent, loose bowel movements)

- Vomiting (throwing up)
- Inflammation (redness, swelling) inside the mouth that sometimes occurs as an allergic reaction, can also result from infection or virus
- Anorexia (loss of appetite for food)
- Hand and foot syndrome: recurrent painful swelling of the hands and feet
- Anemia (lack of red blood cells- may make you feel tired or weak)
- Rash

Less Likely:

- Fever
- Shortage of granulocytes in blood, increased risk of infection
- Reduced platelets- may make you more likely to bruise or bleed
- Upset stomach, trouble digesting food with discomfort after meals
- Dizziness
- Dehydration: condition that results from excessive loss of body water

Rare:

- Constipation (decreased frequency of bowel movements)
- Headache
- Cough

Rare, But Serious:

- Heart attack, death of heart muscle, or not enough blood going to the heart
- Abdominal pain
- Injury to the nerves that supply sensation to the arms and legs
- Difficulty breathing, shortness of breath
- Chest pain due to decreased oxygen being supplied to the heart
- Abnormally high concentrations of the bile pigment bilirubin in the bloodstream
- Decrease in kidney function

Possible Side Effects of Radiation Likely:

- Tiredness
- Loss of appetite
- Nausea and/or vomiting
- Weight loss
- Diarrhea
- Decreased number of white blood cells (may make you more vulnerable to infection which could be serious even leading to death)
- Lower number of red blood cells (may make you short of breath, weak, fatigued or tired)
- Lower number of platelets (may result in easy bruising or bleeding)
- The development of a red rash in the region where you received radiation which may occur within a few days, or as long as a few years after you finish your radiation therapy. This is also called "Radiation Recall Reaction".

Less Likely:

- Some portion of one or both kidneys, the liver, and spinal cord may receive radiation. Though this treatment is not likely to cause any clinical problems as far as these organs are concerned, there is a rare possibility of kidney, liver, or spinal cord damage as a result of the radiation.
- Intestinal scarring requiring surgery or hospitalization
- Abdominal pain or bleeding

The risks of **Surgery** will be reviewed with you in a separate consent form prior to surgery.

Side Effects of Pembrolizumab

Pembrolizumab, which is approved in the USA and some other countries, is available by prescription to treat several different cancers, but may not be approved to treat your type of cancer.

Pembrolizumab works by helping your immune system to fight your cancer.

However, pembrolizumab can also cause your immune system to attack normal organs and tissues in your body and can affect the way they work, which can result in side effects. These side effects may be serious (i.e., causing hospitalization or be life- threatening), and may result in death and/or may occur after you stop taking pembrolizumab. These side effects can affect more than one of your normal organs and tissues at the same time.

Very Common

Out of 100 people who received pembrolizumab, 20 or more people may have the following:

- Itching of the skin
- Loose or watery stools
- Cough

Common

Out of 100 people who receive pembrolizumab, at least 5 but less than 20 people may have the following:

- Joint pain
- Rash
- Fever
- Back Pain
- Pain in your belly
- Loss of skin color
- Not enough thyroid hormone so you may feel tired, gain weight, feel cold, have infrequent or hard stools (hypothyroidism)
- Low levels of salt in the blood that may cause you to feel tired, confused, have a headache, muscle cramps and/or feel sick to your stomach (hyponatremia)

Uncommon

Out of 100 people who receive pembrolizumab, at least 1 but less than 5 may have the following:

- Inflammation of the lungs, so you may feel short of breath and cough (pneumonitis)
- Too much thyroid hormone so you may feel anxious, feel angry, have trouble sleeping, feel weak, tremble, sweat, feel tired, have loose and watery stools (hyperthyroidism)
- Infusion reaction, where you may feel dizzy or faint, feel flushed, get a rash, have a fever, feel short of breath, experience a decrease in your blood pressure at the time of receiving your infusion (IV) or just after, or have pain at the site of infusion
- Inflammation of the bowels/gut, which may cause severe pain in your belly with loose or watery stools, and black, tarry, sticky stools or stools with blood or mucus (colitis)
- Inflammation of the skin so you may have peeling of the skin, itchiness, and/or skin redness. The skin inflammation (i.e. peeling, itching and redness) could also be widespread throughout your body. More severe skin reactions may involve the inside of your mouth, the surface of your eye and genital areas, and/or may cause the top layer of your skin to peel from all over your body which can cause severe infection (Severe skin reactions, including Stevens-Johnson syndrome or toxic epidermal necrolysis)

Rare

Out of 100 people who receive pembrolizumab, less than 1 person may have the following:

- Inflammation of the nerves that may cause pain, weakness or tingling your hands and feet, and may spread to your legs, arms and upper body leading to severe muscle weakness and possible temporary paralysis (Guillain-Barre syndrome)
- Inflammation of the muscles so you may feel weak or have pain in your muscles (myositis)
- Inflammation of the pancreas (a gland in your abdomen that controls sugar levels) so you may have severe upper abdominal pain that may move to your back, feel sick to your stomach, and vomiting that gets worse when you eat (pancreatitis)
- Inflammation of the eye so you may have eye redness, blurred vision, sensitivity to light, have eye pain, see floaters or have headaches (uveitis)
- Inflammation of the liver that may make you feel sick to your stomach and vomit, feel like not eating, feel tired, have a mild fever, have a pain in the right side of your belly, yellow eyes and skin, and dark urine (hepatitis)
- Inflammation of the pituitary gland (a gland in the head), which may cause you to feel sick to your stomach or have headaches, changes in your behavior, double vision, few to no menstrual cycles, weakness, vomiting and dizziness or fainting (hypophysitis)
- Adrenal glands (glands on top of the kidneys) that may not make enough hormone, which could cause tiredness, weight loss, muscle weakness, feeling faint, having joint, muscle and belly aches, nausea, vomiting, diarrhea, fever, salt craving, and sometimes darkening of the skin like a suntan (adrenal insufficiency)
- Type 1 diabetes, a condition that can cause too much sugar in your blood, feeling thirstier than usual, frequent urination and weight loss. You are likely to need regular insulin shots
- Inflammation of the kidney so you may pass less urine or have cloudy or bloody urine, swelling and low back pain (nephritis)

- Inflammation of the middle layer of your heart wall that may cause your heart to have difficulty pumping blood throughout your body, which can cause chest pain, shortness of breath and swelling of the legs. You may experience a fast or irregular heartbeat that may cause dizziness or fainting (myocarditis)
- Inflammation of the thyroid gland, an organ that makes and stores thyroid hormones. This condition may lead to change in your heart rate, blood pressure, body temperature, and the rate at which food is converted into energy (thyroiditis)
- A condition that may make you feel weak and tired and may cause drooping of the eyelids, blurred or double vision, difficulty swallowing, slurred speech, weakness in your arms and legs, or difficulty breathing (myasthenic syndrome/myasthenia gravis including exacerbation)
- The formation of small clusters of immune cells (called granulomas) in parts of your body such as your lymph nodes, eyes, skin, or lungs (sarcoidosis)
- Inflammation of the brain with confusion and fever. This may also include: disorientation, memory problems, seizures (fits), changes in personality and behavior, difficulty speaking, weakness or loss of movement in some parts of your body, and loss of consciousness (encephalitis)
- Inflammation of the spinal cord with pain, numbness, tingling, or weakness in the arms or legs, bladder or bowel problems including needing to urinate more frequently, urinary incontinence, difficulty urinating, and constipation (myelitis)
- Inflammation of the blood vessels (vasculitis). Symptoms will depend on the particular blood vessels that are involved in the inflammatory process, for example; if it is your skin, you may get a rash. If your nerves are not getting enough blood, you could have numbness and weakness. You may also experience fever, weight loss, and fatigue.
- Low levels of parathyroid hormone (a hormone made by 4 tiny glands in your neck) which may result in low blood calcium and cause muscle cramps or spasms; fatigue or weakness; numbness, tingling or burning in your fingertips, toes or lips (hypoparathyroidism)
- Inflammation of the stomach (gastritis). You may have pain in your belly, feel full, or sick to your stomach. You may also experience nausea, vomiting or loss of appetite
- Low number of red blood cells (cells that carry oxygen) due to destruction of red blood cells (hemolytic anemia). You may feel weak, tired, lightheaded, short of breath, or have a fast heartbeat. You may also experience difficulty with physical exercise, pale or yellow skin, dark urine, or fever
- Not enough pancreatic enzymes (proteins that break down food) that leads to poor digestion of food (exocrine pancreatic insufficiency). You may have bloating, gas, discomfort in your belly, diarrhea, abnormal stool that is oily, or weight loss
- Inflammation of the protective sac surrounding your heart (pericarditis), which can cause sharp chest pain and shortness of breath (especially when lying flat), fever, and a fast or irregular heartbeat. In severe cases, your heart may have difficulty pumping blood throughout your body.

Additionally, since pembrolizumab as was approved in September 2014, the following side effects have been reported by people receiving pembrolizumab. These side effects were voluntarily reported from a group of people of unknown size. It is not possible to estimate the

frequency of these side effects:

- Inflammation of the joints which may include joint pain, stiffness and/or swelling (arthritis)
- Severe responses of the immune system that causes the body to attack its own blood cells, spleen, liver, lymph nodes, skin and brain. This may include fever, rash, inflammation of the liver, yellowing of the skin, an enlarged liver and spleen, low blood counts, and enlarged lymph nodes. The nervous system may also be affected and cause confusion, seizures, and even coma (hemophagocytic lymphohistiocytosis)
- Changes in eyesight, eye pain, whitish patches on the skin and hearing loss (Vogt-Koyanagi-Harada syndrome)
- Inflammation and scarring of the bile ducts (tubes that carry digestive fluid that is made in the liver). This can cause symptoms similar to those seen with inflammation of the liver (hepatitis) such as pain in right side of your belly, yellow eyes and skin, feeling tired, and itching (sclerosing cholangitis)
- Inflammation or swelling of the nerve fibers of the eye which send visual information from your eye to your brain. This health condition often has a sudden onset of vision loss, loss of color vision, pain when moving your eyes, and/or loss of peripheral vision. It may affect one or both eyes at the same time (optic neuritis)

If you have had an allogeneic stem cell transplant (a procedure in which a person receives blood-forming stem cells from a donor), you may experience graft versus host disease (GvHD), which may include diarrhea, skin rashes, and liver damage, **after receiving pembrolizumab**. Sometimes this condition can lead to death.

If you have had a solid organ transplant (for example, if you have received a kidney or heart transplant), you may experience rejection of the transplanted organ. Your doctor will monitor you and should tell you what signs and symptoms you should report depending on the type of organ transplant that you have had.
Patients treated with pembrolizumab **BEFORE** going on to receive an allogeneic stem cell transplant (a procedure in which a person receive blood–forming stem cells from a donor), should inform their transplant physicians that they have received pembrolizumab in the past.
In patients with any hematologic malignancy (cancer of the blood like Hodgkin lymphoma, multiple myeloma): there is a potential for an increased risk of severe complications following allogeneic stem cell transplant in patients who previously received pembrolizumab **BEFORE** an allogeneic stem cell transplant.
Reports of clotting of blood within the liver and severe graft versus host disease (which can include skin, liver, and gastrointestinal symptoms), including death, have been received for patients who received pembrolizumab **BEFORE** an allogeneic stem cell transplant.

Patients with multiple myeloma who were treated with pembrolizumab in combination with either pomalidomide or lenalidomide (drugs related to thalidomide which affect the body's immune system) and dexamethasone (a steroid) had an increased number of side effects and deaths as compared to patients who received only dexamethasone and either pomalidomide or lenalidomide.

Reproductive risks

You should not become pregnant or father a baby while on this study because the drugs and radiation treatment in this study can affect an unborn baby. Women who are able to have children will have a pregnancy test before beginning treatment. Women should not breastfeed a baby while on this study. It is important you understand that you need to use birth control for as long as you are receiving treatment on this study and for 120 days after completion of all treatment to prevent pregnancy or fathering a child. Check with your study doctor about what kind of birth control methods to use. Some methods might not be approved for use in this study. The treatment in the study may make you unable to have children in the future. Women of childbearing age can ask their doctor for information about pre-treatment or post-treatment reproductive or fertility options prior to agreeing to participate in the study.

Possible Risks Related to Reproductive health/sexual activity
Researchers have not studied the effect of the study drug, pembrolizumab, on human sperm and eggs. They also do not know the effects on the developing fetus using the study drug during pregnancy and the risk of birth defects from use of pembrolizumab. Therefore, both men and women should not attempt pregnancy and women should not be pregnant or breast-feeding while taking part in this study and for at least 120 days after your last dose of the study drug pembrolizumab.

If sexually active, both men and women should use an effective method of birth control while taking the study drug. Barrier contraceptives (condoms or diaphragm) with spermicide, intrauterine devices (IUDs), hormonal contraceptives, oral contraceptive pills, surgical sterilization, and complete abstinence are examples of effective methods. Only methods that use condoms provide reasonable/true protection against sexually transmitted diseases. If you or your partner become pregnant while taking the study drug, you must tell your study nurse/doctor immediately. You may have to stop the study drug. Your doctor will discuss other treatment options with you if you stop the study drug.

A woman should not breast-feed a baby while in this study because pembrolizumab may enter the breast milk and possibly harm the child.

If you are a woman capable of bearing children, you will have a pregnancy test before you can participate in this study. If at any time during the study or within 120 days after your last dose of the study drug pembrolizumab you suspect that you have become pregnant, please notify the study doctor immediately.

Male participants should immediately inform the study doctor if your partner becomes pregnant during the study, within 120 days after your last dose of the study drug pembrolizumab.

Are there any benefits for you if you choose to take part in this research study?
Taking part in this study may or may not improve your health or allow you to live longer. The information from this study will help doctors learn more about pembrolizumab as a treatment for gastric cancer. This information could help other people who have a similar medical condition in the future.

What are your alternatives if you don't want to take part in this study?
You do not have to take part in this research study. If you decide not to take part in this study,

you have other choices. Instead of being in this study, you can:

- Choose to have the usual approach to treatment described above without being in a study
- Take part in another study
- Get 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.

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

How will you know if new information is learned that may affect whether you are willing to stay in this research study?
During the study, your study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study. When informed of this new information, if you agree to continue in the study, your doctor will ask you to sign an updated Informed Consent Form**.**

Will there be any cost to you to take part in this study?
You will have tests and procedures that are part of your regular medical care (not part of the research), including the treatment with surgery, capecitabine and radiation therapy. You or your insurance company or third party provider will be responsible for these costs, including co-payments and deductibles. Some health insurance plans will not pay the costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for.

The study will provide the drug pembrolizumab at no charge to you while you take part in this study. The study does not pay for the cost of getting the study drug ready and giving it to you intravenously (in a vein). You or your insurance company will pay for this procedure.

You will not need to pay for tests and procedures that are done just for this research study.

Taking part in this study may or may not cost your insurance company more than the cost of getting regular treatment. If your insurance does not pay, you will be responsible for the charges of your regular medical care. Before you decide to participate in the study, you should check with your health insurance company to find out exactly what it will pay for.

If you have any questions about insurance coverage, including any out of pocket expenses you might incur, or which laboratory or facilities you are allowed to have tests at, a financial counselor will be made available to you upon request.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at: http://www.cancer.gov/clinicaltrials/learningabout/payingfor

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 paid to take part in this study?

You will not receive any payment for your participation in this study.

Who might benefit financially from this research?

This research study is supported by money from Merck & Co. In addition, Dr. Salma Jabbour, the investigator leading this study and Dr. Howard Hochster, one of the investigators on this study receive funding from Merck & Co. for work that is not a part of this study. These activities may include consulting, advisory boards, giving speeches, or writing reports.

How will information about you be kept private or confidential?

All efforts will be made to keep your personal information in your research record confidential, but total confidentiality cannot be guaranteed. Your personal information may be given out if required by law.

Information about your cancer and treatment will be collected from your medical record for the study. The information will be with a study identification number and stored in a secured electronic file. The electronic file is password protected and accessible only to authorized study personnel.

If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

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

What will happen if you are injured during this study?

Subjects in this study will be exposed to certain risks of personal injury in addition to those associated with standard forms of treatment, which were discussed in the Risk and Discomforts section of this consent form. In addition, it is possible that during the course of this study, new adverse effects of surgery, capecitabine, pembrolizumab and radiation therapy that result in personal injury may be discovered. The University will make appropriate referrals for medical and/or dental treatment for subjects who sustain personal injuries or illnesses as a direct consequence of participation in the research. The subject's health insurance carrier or other third-party payer will be billed for the cost of this treatment; provided that the University shall not submit to federally funded programs, e.g., Medicare, Medicaid or CHAMPUS, for reimbursement first if submission to such programs is prohibited by law. No financial compensation will be provided by the University and no other type of assistance is available from the University.

You are not giving up any of your legal rights by signing this informed consent form or by taking part in this research study.

What will happen if you do not wish to take part in the study or if you later decide not to stay in the study?

You can decide to stop at any time. If you decide to stop for any reason, you must let the study

doctor know as soon as possible so you can stop safely.

If you do not want to enter the study or decide to stop participating, your relationship with the study staff will not change, and you may do so without penalty and without loss of benefits to which you are otherwise entitled.

It is important to tell the study doctor if you are thinking about stopping so any risks from the study can be evaluated by your doctor. Another reason to tell your study doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

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

If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study, however, the FDA requires that any information collected up to the point of your withdrawal cannot be removed from the study.

You may also withdraw your consent for the use of data already collected about you, but you must do this in writing to:
Salma Jabbour, MD
Rutgers Cancer Institute
195 Little Albany Street
New Brunswick, NJ 08901
Telephone: (732) 235-2465

At any time, the study doctor can take you out of this study because it would not be in your best interest to stay in it, even if you are willing to stay in the study.

If you decide to withdraw from the study for any reason, you may be asked to return for at least one additional visit for safety reasons.

Who can you call if you have any questions?
If you have questions, concerns or complaints about the research, wish more information or if you feel you may have suffered a research related injury, you can contact the Principal Investigator:
Salma Jabbour, MD
Rutgers Cancer Institute
195 Little Albany Street
New Brunswick, NJ 08901
Telephone: (732) 235-2465

If you have questions, concerns, problems, information or input about the research or would like to know your rights as a research subject, you can contact the Rutgers IRB Office at: (973) 972-3608 or (732) 235-9806 or (732) 235-2866, or email us at IRBOffice@research.rutgers.edu, or write us at 335 George Street, Liberty Plaza Suite 3200, New Brunswick, NJ 08901

What are your rights if you decide to take part in this research study?
You have the right to ask questions about any part of the study at any time. You should not sign

this form unless you have had a chance to ask questions and have been given answers to all of your questions.

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

Request to Store Leftover Tissue* Samples for Future Research Use

*We use the term "tissue" to refer to specimens such as blood, urine, existing already taken tumor tissue from a previous surgery before entering this study, or tissue taken from a surgery as part of this research study.

We ask your permission to store leftover tissue samples collected from you during a previous surgery and/or during this study for future research. Following are details about our request. Please know that you may still participate in the main study even if you say no to this request to store tissue for future research.

How and where will your leftover tissue be stored and by whom?

Your leftover tissue samples will be stored in the Rutgers Cancer Institute Biorepository Service (BRS), which is owned and operated by the Rutgers Cancer Institute. The repository is at 195 Little Albany Street, New Brunswick, NJ, 08903.

The purpose of the repository is to store leftover tissue samples to be used for future research to be conducted by the Principal Investigator and the research staff at the Rutgers Cancer Institute. The goal of the research is to better understand and develop better means to prevent, diagnose and treat disease.

All of the subjects in this study will be asked to allow leftover tissue to be stored and used for future use in the repository. The more samples and health information available in storage, the more useful the repository will be for medical research.

How will samples be collected?

Only the leftover tissue that was collected during a previous surgery and/or as a part of this research study and research blood would be stored and used for future use.

Psychological or Social Risks Associated with Loss of Privacy:

While the databases developed for this project will be coded to protect your personal information, people may develop ways in the future that would allow someone to link your medical information back to you. It is also possible that there could be violations to the security of the computer systems.

There also may be other privacy risks that we have not foreseen.

What are the benefits of participation?

You will not benefit personally from providing tissue samples for this tissue bank because research usually takes a long time to produce meaningful results. However, your participation may help investigators understand, prevent, or treat the diseases and conditions studied in the future.

How will information about you and your tissue samples be kept private and confidential?
Information obtained from this research with material obtained from your tissue sample(s) will be kept confidential so that neither the investigator nor the Sponsor can link your individual research results with your identity.

Your sample(s), and materials derived from your sample(s), will be given a code number, and only information related to your age, sex, race, health condition and other relevant clinical information collected in the main study will be linked with the sample's code number. Your name, date of birth, address, or other personal identifying information, will not be linked with the sample(s) you give.

Is there other important information to consider?
Yes. There is no cost to you to allow us to store and use your tissue and information for future research. Nor will you be paid to participate in this repository. Should any products or services result from research using your samples and information, there is no plan to share any of the profits with you.

The research we are doing is only a stepping stone in understanding disease. It may take a long time for our research to produce useful health-related information. Therefore, tests done for our research using your samples and information will not be useful in directing your medical care. Information from our research will not be returned to you, your family members, your doctor, or outside parties. It is possible, however, that members of regulatory authorities, such as the U.S. Food and Drug Administration, Rutgers University Institutional Review Board, or other persons required by law may be allowed to look at this information.

What are your rights if you agree to the storage and use of your tissue for future research?
You have the right to ask questions about any part of our storage and future research at any time. You should not sign this form unless you have a chance to ask questions and have been given answers to all of your questions. Your participation in this part of the study is voluntary. You do not have to participate. If you do, you can change your mind at any time.

What are the procedures for withdrawing consent?
If you agree to allow your tissue to be stored for future research at the Rutgers Cancer Institute Biorepository Service, but change your mind later, you can write to your study doctor, Salma Jabbour, MD, Rutgers Cancer Institute, 195 Little Albany Street, New Brunswick, NJ 08903 and tell her to destroy any remaining tissue samples and data that are currently being stored in the repository.

However, please note that it may not be possible to destroy samples, information and data created from your samples that may have already been used in research studies prior to your request. The Rutgers Cancer Institute will keep records linking your identity with the tissue sample(s) indefinitely. Until those records are destroyed, you may ask that your tissue sample(s) and materials obtained from your sample(s) be destroyed.

Permission to Collect Leftover Tissue:
Please read each sentence below and think about your choice. After reading each sentence, initial next to "Yes" or "No". If you have any questions, please talk to your doctor or nurse, or call our

research review board at 732-235-9806.

No matter what you decide to do, it will not affect your care or your participation in the main study.

If there is leftover research tissue (blood and tumor) collected for this study, the leftover tissue may be collected for future research to learn about, prevent or treat cancer

_____YES _____NO

Permission to Contact You with Additional Requests to Participate in Research
Please tell us if we may contact you in the future to tell you about other ways you may participate in this research or other research we are conducting by initialing next to your choice.

The investigators may contact me in the future to ask me to take part in more research.

_____YES _____NO

What are your rights if you agree to the use of your blood/tissue for other types of research for future research?
You understand that you have the right to ask questions about any part of the future study at any time. You understand that you should not sign this form unless you have had a chance to ask questions and have been given answers to all of your questions.

A federal law (Genetic Information Non-Discrimination Act, GINA) will help lower the risk from health insurance or employment discrimination on the basis of genetic information. The federal law does not include other types of misuse by life insurance, long-term care or disability insurance. If you want to learn more about the GINA Law, you can find information about it on the internet or ask the study staff. In addition to the federal law, some states have laws that also help protect against genetic discrimination.

Since some genetic variations can help to predict the future health problems of you and your relatives, this information might be of interest to health providers, life insurance companies, and others. Therefore, your genetic information potentially could be used in ways that could cause you or your family economic stress.

There are state and federal laws that protect against genetic discrimination. A federal law, the Genetic Information Nondiscrimination Act makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways: (1) health insurance companies and group health plans may not request your genetic information that we get from this research; (2) health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums; and (3) employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Authorization to use your health information for future research purposes
Because information about you and your health is personal and private, it generally cannot be used in future research studies without your written permission.

If you agree to allow us to use your health information for future research, you are permitting us to share this information with our research collaborators at Rutgers University.

_____YES _____NO

PERMISSION (Authorization) TO USE OR SHARE HEALTH INFORMATION THAT IDENTIFIES YOU FOR A RESEARCH STUDY

Information about you and your health is personal and private, so this information generally cannot be used in research without your written permission. The next few paragraphs tell you about how researchers want to use and share your health information in this research study. Your information will only be used as described here or as allowed or required by law. Ask questions if you do not understand any part of the research or the use of your health information. If you sign this consent form, you agree to let the researchers use your information in the research and share it with others as described below.

What is the purpose of the research and how will my information be used?
You are being invited to take part in this research study which is described at the beginning of this form. The purpose of collecting and using your health information for this study is to help researchers answer the questions that are being asked in the research.

What information about me will be used?
If you choose to be in this study, the study doctor will get your personal and medical information. This information may include:

- All information in a medical record
- Results of physical examinations
- Medical history
- Current and past medications or therapies
- Lab tests, or certain health information indicating or relating to a particular condition as well diaries and questionnaires
- Records about study medication or drugs
- Records of blood tests
- Results of chest x-ray
- Results of imaging studies, including: MRI, CT and X-ray scans
- Information about any side effects you may experience while on study

Who may use, share or receive my information?

The research team may use or share your information collected or created for this study with the following people and institutions:

- Rutgers University investigators involved in the study;

- University Hospital or Robert Wood University Hospital personnel to communicate information necessary for health care operations;
- The Rutgers University Institutional Review Board and Compliance Boards
- The Office for Human Research Protections in the U.S. Dept. of Health and Human Services
- Merck & Co., Inc., the company that supplies Pembrolizumab for use in this study

Those persons or organizations that receive your information may not be required by Federal privacy laws to protect it and may share your information with others without your permission, if permitted by the laws governing them.

Will I be able to review my research record while the research is ongoing?
No. We are not able to share information in the research records with you until the study is over. To ask for this information, please contact the Principal Investigator, the person in charge of this research study.

Do I have to give my permission?
No. You do not have to permit use of your information. But, if you do not give permission, you cannot take part in this research study. (Saying no does not stop you from getting medical care or other benefits you are eligible for outside of this study.)

If I say yes now, can I change my mind and take away my permission later?
Yes. You may change your mind and not allow the continued use of your information (and to stop taking part in the study) at any time. If you take away permission, your information will no longer be used or shared in the study, but we will not be able to take back information that has already been used or shared with others. If you say yes now but change your mind later for use of your information in the research, you must write to the researcher and tell him of your decision:
Salma Jabbour, MD
Rutgers Cancer Institute
195 Little Albany Street
New Brunswick NJ 08903

How long will my permission last?
There is no set date when your permission will end. Your health information may be studies for many years.

Where can you get more information?
You may call the National Cancer Institute's Cancer Information Service at:
Voice: 1-800-4-CANCER (1-800-422-6237)

You may also visit the NCI Web site at http://cancer.gov/
For NCI's clinical trials information, go to: http://cancer.gov/clinicaltrials/
For NCI's general information about cancer, go to http://cancer.gov/cancerinfo/
If you do not have access to a personal computer, you may access these websites and other information at a computer in the Resource and Learning Center on the second floor of the Cancer Institute at no cost to you.

AGREEMENT TO PARTICIPATE

I have read this entire form, or it has been read to me, and I believe that I understand what has been discussed. All of my questions about this form or this study have been answered.

I agree to take part in this study.

Subject Name:_____

Subject Signature:_____ Date: _____

FOR NON-ENGLISH SPEAKING SUBJECTS:

Signature of Reader/Translator If the Subject Does Not Read English Well:

The person who has signed the short form, _____, does not read English well. You read English well and are fluent in _____ (*name of the language)*, a language that the subject (his/her parent(s)/legal guardian) understands well. You understand the content of this consent form and you have translated for the subject (his/her parent(s)/legal guardian) the entire content of this form. To the best of your knowledge, the subject (his/her parent(s)/legal guardian) understands the content of this form and has had an opportunity to ask questions regarding the consent form and the study, and these questions have been answered (his/her parent(s)/legal guardian).

Reader/Translator Name:_____

Reader/Translator Signature:_____ Date:_____

Witness Name:_____

Witness Signature:_____ Date:_____

Signature of Investigator/Individual Obtaining Consent:
To the best of your ability, you have explained and discussed the full contents of the study including all of the information contained in this consent form. All questions of the research subject and those of his/her parent or legal guardian have been accurately answered.

Investigator/Person Obtaining Consent:_____

Signature:_____ Date: _____