COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT

YALE UNIVERSITY SCHOOL OF MEDICINE – YALE-NEW HAVEN HOSPITAL: SMILOW CANCER HOSPITAL

200 FR. 4 (2014-11)

Study Title: A Phase II Study of Pembrolizumab as Monotherapy for Metastatic Triple-Negative Breast Cancer (mTNBC)

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Invitation to Participate and Description of Project

You are invited to take part in a research study. The research study is designed to test the anti-tumor activity, safety, and tolerability of the research study drug, pembrolizumab (MK-3475), in subjects with Metastatic Triple-Negative Breast Cancer (mTNBC).

You have been invited to take part because you have been diagnosed with Metastatic Triple-Negative Breast Cancer (mTNBC).

In order to decide whether or not you wish to be a part of this research study you should know enough about its risks and benefits to make an informed decision. This consent form gives you detailed information about the study, which a member of the research team will discuss with you. This discussion should go over all aspects of this research: the purpose and nature of the research study, the procedures that will be performed, the risks of the study drug(s) and procedures, possible benefits, possible alternative treatments, your rights as a participant and other information about the research study. You should take whatever time you need to discuss the research study with your physician and family. The decision to participate or not is yours. Once you understand the study, you will be asked if you wish to participate; if so, you will be asked to sign and date where indicated on this form.

If you choose to participate, you will be told of any significant new findings that develop during the course of your participation in this study that may affect your willingness to continue to participate.

The research study is being sponsored by Merck Sharp & Dohme Corp. Merck Sharp & Dohme Corp. is called the Sponsor and Yale University is being paid by Merck Sharp & Dohme Corp. to conduct this research study. Dr. Lajos Pusztai is the principal investigator of this study at Yale Cancer Center.

Purpose

The purpose of this study is to test the anti-tumor activity, safety, and tolerability of the research study drug, pembrolizumab (MK-3475), in subjects with Metastatic Triple-Negative Breast Cancer (mTNBC).

The study drug that will be used in this research study, pembrolizumab (MK-3475), is investigational. This means it has not been approved for commercial use by the United States Food and Drug Administration (FDA) in your type of cancer. Pembrolizumab (MK-3475), has been approved for use in certain types of melanoma and lung cancer; however, it has not been approved for Metastatic Triple-Negative Breast Cancer (mTNBC).

It is expected that approximately 285 subjects will participate in this study at approximately 60 sites around the world. It is expected that approximately 15 subjects will be enrolled at Yale Cancer Center.

Study Procedures

Tests and procedures that would be performed for your regular cancer care whether you are on this study or not, are called "standard of care." All of the tests and procedures listed below that will be performed at your study visits, should you choose to participate in this study, are standard of care unless noted with an asterisk (*).

Screening Period

If you agree to participate and sign and date this form, you will need to undergo a series of tests and procedures to determine if you are eligible to participate in the research study. You will come to the study site for screening tests and it is possible that more than one screening visit may be needed.

There may be reasons why you are not allowed to take part in this study. Some of these reasons include:

- You are less than 18 years old.
- You do not have metastatic triple negative breast cancer as assessed by a central vendor.
- You have not provided a newly obtained tumor tissue sample for biomarker (PD-L1) analysis or the sample does not qualify you to enroll.
- You have cancer which cannot be measured by radiological exam.

- You have not demonstrated adequate organ function in lab results.
- You are currently participating and receiving study therapy or have participated in another research study within 4 weeks of the first dose of study drug.
- You have an active autoimmune disease (an illness that occurs when your tissues are wrongly attacked by your own immune system) that required treatment within the last 2 years or a history of severe autoimmune disease or a syndrome that requires steroids or other drugs to suppress your immune system.
- You have an immunodeficiency or are receiving steroids (drugs used to relieve swelling and inflammation) or any other drug to suppress your immune system within 7 days prior to your first dose of study drug.
- You have had anti-cancer therapies within at least 2 weeks prior to Day 1 of the study
- You have unresolved side effects from anti-cancer therapies taken within at least 2 weeks of the first dose of study drug.
- You have another type of cancer that has been treated or became worse during the last 5 years
- You have known active or symptomatic central nervous system (brain) tumor and/or carcinomatous meningitis.
- You have active or a history of (non-infectious) pneumonitis (inflammation of lung tissue), which required steroid drug or history of interstitial lung disease.
- You have an active infection requiring systemic therapy.
- You have a known psychiatric (mental) or drug or alcohol abuse disorder.
- You are pregnant, trying to become pregnant, or breastfeeding during the course of the trial and through 120 days after your last dose of study drug.
- You are a male who is expecting to father a child during the study and through 120 days after your last dose of study drug.
- You have prior therapy with an anti-PD-1, anti-PD-L1, or anti-PD-L2 agent or previously participated in Merck Pembrolizumab (MK-3475) clinical trials.
- You have HIV or active Hepatitis B or Hepatitis C.

  *Positive hepatitis and/ or HIV test results must be reported to the Department of Health as per Connecticut State Law. If you do not wish to have a positive hepatitis and/ or HIV test result reported to the Department of Health, you should not participate in this research study.
- You have received a live vaccine within 30 days of starting the study drug.
- You have an immediate family member (e.g., spouse, parent/legal guardian, sibling, or child) who is directly involved with this trial.
- You have received any chemotherapy or other treatment targeting certain cancer pathways for metastatic breast cancer (Cohort B only).

The study doctor or staff will discuss these and any other reasons why you may not be allowed to enter the study.

Treatment Period

You may be in the treatment phase of the study up to about 3 years and then followed for as long as 1) your disease is not getting worse, 2) you do not receive another anticancer treatment, and 3) you do not have bad side effects.

If your disease gets worse (and you are not eligible for the second course phase of this study) or you need to change treatment you will be contacted by telephone at least every 3 months for survival follow up. The Sponsor may request survival status be assessed at additional time points during the course of the study.

The following is a list of evaluations that you will undergo and instructions to follow during the treatment period of the study:

- Visit the study doctor as instructed. Each study therapy cycle is about 3 weeks. The study doctor or staff will discuss with you when and on which days to report to the clinic.
- If you agree to take part in this study, it is very important that you tell your study doctor before starting on this study about all of the medicines you are taking or have recently taken (over-the-counter medications, supplements, prescription medications, or illegal drugs). The reason this is important is that some medicines can change the way your body handles other medicines and this can increase the risk of side effects from the study drug. In addition, please talk with the study doctor before you begin taking any new medications or supplements during this study. Your study doctor will look at the medicines you are currently taking to make sure you are allowed to take them while on the study. You may be asked to change some of the medicines you are taking. If you need to take a medicine that is not allowed and it cannot be replaced with another medicine, you will not be asked to stop taking it; however, you will not be able to take part in this study.
- If your blood tests show that you have liver lab results that are not normal, the study doctor or staff will ask you to provide additional samples of blood for testing to find out why your liver lab results are not normal. If you do decide to provide the samples, the study staff will discuss with you the amount of the additional samples of blood that will be taken and the tests that will be performed on the blood.
- The tests that may be performed include HIV and viral hepatitis tests to find out if HIV or hepatitis is the reason your liver lab results are not normal. Depending on the region where you live, you may need to sign another consent form to have these tests done. (see previous page regarding Connecticut state law)

- The results of all of your blood tests, just like all other laboratory test results, will be provided to the Sponsor. Positive HIV and Viral Hepatitis test results may be reportable to local health authorities according to local laws.
- It is your decision whether you provide the additional samples and have these tests performed. However, if you decide not to provide the additional samples and have the tests done, you may need to leave the study for your own safety (as the cause of your abnormal liver lab results may not be able to be determined without them).
- You will be asked to provide a tumor sample* from a previous biopsy or surgical procedure (archival tumor sample), if available. You will also be asked to provide a newly obtained tumor biopsy tissue sample* before the first dose of study drug. This sample will be tested to ensure it can be evaluated for the specific biomarkers to be tested in this study. Additional newly obtained tumor biopsy tissue samples during and after you receive the study drug will be requested but are not required. Your tumor samples may also be used for the analysis of additional biomarkers to investigate ways that the study drug does or does not work to shrink tumors. Other additional biomarkers which may impact how individuals respond to the study drug may also be analyzed. Any sample left over after these tests will be stored for future research if you consent to the optional Future Biomedical Research (FBR) sub-study. These results are for research only. Since these tests are exploratory research only, they will have no clear implications about you or your family's medical conditions. The results of the testing will not be returned to you.
- Agree to have your tumor sample tested by a laboratory for a protein that may be on the surface of your tumor called "PD-L1"*. This test will look to see if your tumor's tissue has certain features which may help scientists better understand cancer. This test may help scientists understand why your cancer did or did not respond to the study drug. Since this test is investigational, the accuracy of the results cannot be guaranteed. As with any investigational test, there is a potential for false positive or false negative results that could incorrectly include you in or exclude you out from this investigation. This testing may be repeated after the study is over at the request of regulatory authorities, but your samples will not be stored for future use unless you consent to future biomedical research.
- You will be asked to provide blood samples to be used for studying biomarkers in the blood*. These samples will be used to analyze biomarkers to discover ways that the study drug does or does not work to shrink tumors. Additional biomarkers which may impact how individuals respond to the study drug may also be analyzed. Any sample left over will be destroyed once all study related needs have been met. Your sample will not be saved for future testing. The results of the testing will not be returned to you.
- Take study drug* as instructed.
    - Pembrolizumab will be administered as a 30 minute intravenous (IV) infusion, into one of your veins, on Day 1 of every 3 week (21 days) treatment cycles. The time between doses may increase if you experience bad side effects.

Tumor Evaluations:
Before you start study drug and during the study, you will have radiographic assessments of your cancer by Computed Tomography (CT) Scan and/or Magnetic Resonance Imaging (MRI), and/or bone scan/x-ray.

Radiographic assessment of your cancer will be done before you start the study drug and then every 9 weeks after you start the study drug in the first year and every 12 weeks after one year.
If the assessment of your cancer by CT or MRI shows that your cancer may have worsened, you may be asked to have another radiographic assessment performed at least 4 weeks later to confirm the worsening. The study doctor will discuss your options during the period between scans, which may include the following:

- Continue to receive the study drug or;
- Have study drug held until the time that the worsening is confirmed or;
- Discontinue from the study and instead receive an approved, licensed drug, which may shrink your tumor, delay progression of your cancer, provide symptom relief or prolong survival
- There may be approved chemotherapy drugs (chemicals that directly kill cancer cells) that are commonly used for your cancer. Your study doctor will discuss what drugs are approved and available for treatment in your region.

You may be eligible to receive treatment with a different study drug.

If you elect to stay in the study until the confirmation scan, you will not be eligible to receive any of these other medications until the worsening of your disease is confirmed and the study drug is stopped. If the follow up radiographic assessment (after the assessment that first showed worsening of your cancer) shows that the size of your tumor has not increased further and your doctor thinks you are doing well you may be eligible to continue on the study drug after your study doctor has a discussion with the Sponsor.

End of Treatment and Safety Follow-up
You will take the study drug as long as your cancer does not get worse or you do not have bad side effects.

If your cancer has not worsened after 24 months on study therapy or if your tumor goes away, you may stop taking study therapy.

When you stop taking study therapy you will have a study drug discontinuation visit. Additionally, you will be asked to complete a 30-day safety follow-up visit (about 30 days after

your last dose of the study drug or before you start a new treatment for your cancer, whichever comes first) to check if you have any new or on-going side effects.

Your disease status will be monitored every 12 weeks by radiographic imaging.

If at any point during this time your cancer gets worse, you may be eligible to receive an additional 12 months of pembrolizumab during the Second Course Phase. Your doctor will discuss this with you.

Follow-up Period

Imaging and Survival Follow-up

If you stop taking the study drug before your cancer gets worse (disease progression) you will continue to come in for a follow-up visit every 9 weeks in the first year and every 12 weeks after one year to monitor your disease status and to perform additional study related testing (which also may include blood sample collections and tumor imaging) until your cancer gets worse or you start a new treatment for your cancer.

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

Second Course Treatment:

If you stop pembrolizumab after 2 years of treatment or because you had a complete response, you may be eligible for up to one year of additional pembrolizumab therapy if the disease progresses after stopping pembrolizumab. This is called Second Course Phase of pembrolizumab treatment. 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 pembrolizumab and will be retreated at the dose and dose frequency received upon initial treatment with pembrolizumab.

What will happen during the study visits?

When you come in for your study visits, the study doctor or staff may do any or all of the following to measure if the drug is working and/or to monitor your health.

- Give you a subject ID card.
- Administer study drug.
- Review your medical history and health.
- Review the medications you have taken and your current medications.
- Perform a physical exam.
- Collect your vital signs (including your temperature, pulse, breathing rate, and blood pressure).

- Measure your height and weight.
- Perform an electrocardiogram (ECG)* to check your heart.
- Collect blood and urine samples:
    - For safety tests.
    - To perform a pregnancy test if you are a woman able to have children*.
    - To measure the amount of study drug in your body. This process is known as pharmacokinetics (PK)*.
    - To test for natural antibodies made by the body that attach to Pembrolizumab (MK-3475) in your blood*.
    - To test for biomarkers that help researchers understand the relationship between the study drug and its effects on your tumor*.
    - To test for cells in your blood that keep your immune system from working properly*.
- Perform a CT scan, MRI, bone scan or x-ray of your tumor. Imaging of your brain is required at screening*.
- Assess your disease status and ability to perform physical tasks.
- Review any side effects you have had.
- Collect a tumor sample* from a newly obtained biopsy before the start of the trial, and if available, collect a cancer sample from a previous procedure (called “archival tumor tissue”)*. These samples will be used for special studies to evaluate biomarkers thought to be important for cancer response to the study drug.
- Collect added biopsy samples about 9 weeks or at any time point after receiving your first dose of study drug, and again, if the radiology scans show that your disease has worsened. These added samples will be requested but are not required.
- A blood sample will be collected for planned genetic research*. Your blood and tissue samples contain genes, which are made up of DNA (deoxyribonucleic acid) and which serve as the "instruction book" for the cells that make up our bodies. Genetic research is the study of DNA variation. Variation in your DNA can affect the way you respond to drug treatments. The Sponsor will look at variation in your DNA. Your DNA will be used to understand how genetics affect response to the treatment(s) administered. Your genetic information will be analyzed together with the clinical data collected in this study. Your blood may also be used to help develop new tests. The results are for research use only.
- You will also be asked to take part in optional future biomedical research. You will be given a separate informed consent that will describe this research and seek your consent.

Potential Risks, Side Effects, Discomforts and Inconveniences

Risks associated with Pembrolizumab (also known as MK-3475):
While in this study, you may have side effects. Anticipated side effects are listed here. In addition to the risks listed below, there may be risks that are currently unknown. If significant new risks develop during the course of study that might affect your willingness to participate, information will be reported to you as soon as possible. Possible side effects that you may experience during this study will be fully explained to you by the study staff. Please ask as many questions as you want so that you can understand the possible side effects of your specific study drug assignment before you decide whether you want to be in this study. Please ask the study doctor or the study staff to explain any information or words that are not clear to you.

What is known about this study drug?

Pembrolizumab is also known as KEYTRUDA (approved in *USA and several other countries*) and is available by prescription to treat a type of skin cancer called malignant melanoma.

Pembrolizumab/KEYTRUDA is being studied by the Sponsor to see if it is effective in treating more than 30 types of cancer and to see what side effects are associated with its use.

As of 30-Jun-2015, pembrolizumab/KEYTRUDA had been given to about 9400 subjects with various cancers in clinical trials. Men and women with cancer received pembrolizumab, some for up to approximately 1.5 years. Safety was studied across several cancers with different doses: 2 mg/kg every 3 weeks, and 10 mg/kg every 2 or 3 weeks. The side effects seen were similar.

What side effects could the study drug(s) cause?

Very common side effects seen in > 20% of subjects who received pembrolizumab/KEYTRUDA include the following:

- Itching of the skin
- Feeling tired, lack of energy
- Feeling not hungry
- Short of breath
- Cough

Very common side effects seen in ≥10% to 20% of subjects who received pembrolizumab/KEYTRUDA include the following:

- Joint pain
- Fever
- Swelling of legs &/or feet
- Stomach pain
- Sick to your stomach
- Loose or watery stools

- Weakness
- Back pain
- Rash
- Low level of salt in the blood that may cause you to feel tired, confused, headache, muscle cramps or upset stomach
- Infrequent or hard stools
- Vomiting
- Decrease in number of blood cells that carry oxygen which may cause you to feel tired or short of breath
- Loss of skin color

Common serious side effects seen in 1% to 4% of subjects who received pembrolizumab/KEYTRUDA include the following:

- Short of breath
- Feeling tired, lack of energy
- Low level of salt in the blood that may cause you to feel tired, confused, headache, muscle cramps or upset stomach
- Stomach pain
- Decrease in number of blood cells that carry oxygen that may cause you to feel tired or short of breath
- Inflammation of the lungs so you may feel short of breath and cough. Rarely this might lead to death
- Joint pain
- Weakness
- Back pain
- Inflammation of the bowels/gut that can cause stomach pain with loose or watery stools, or stools that are black, tarry, sticky or have blood or mucus
- Feeling not hungry
- Loose or watery stools
- Sick to your stomach
- Fever
- Vomiting

Immune-mediated serious side effects seen in 1% or less of subjects who received pembrolizumab/KEYTRUDA include the following:

- Inflammation of the skin so you may have widespread peeling of the skin, itching, skin redness
- Inflammation of the bowels/gut so you may feel stomach pain with loose or watery stools or stools that are black, tarry, sticky or have blood or mucus

- Inflammation of the lungs so you may feel short of breath and cough. Rarely this might lead to death
- Inflammation of the liver that may cause a poor appetite, feeling tired, mild fever, muscle or joint aches, upset stomach and vomiting, bleeding and bruising more easily than normal, stomach pain, yellow eyes and skin, and dark urine
- Inflammation of the pituitary gland (a gland in the head), which may cause headaches, upset stomach, changes in behavior, double vision, change in eyesight, few to no menstrual cycles, weakness, vomiting and dizziness or fainting. This inflammation of the pituitary gland may cause the adrenal glands (on top of the kidneys) to not make enough hormone causing tiredness, weight loss, muscle weakness, feeling faint, joint, muscle and abdominal aches, nausea, vomiting, diarrhea, fever, salt craving, rapid heart rate, and sometimes darkening of the skin like a suntan.
- Too much thyroid hormone so you may feel anxious, angry, can't sleep, weak, tremble, increased sweating, weight loss, hair loss, tired, have diarrhea
- Too little thyroid hormone so you may feel tired, gain weight, feel cold, voice gets deeper, hair loss, have infrequent or hard bowel movements
- Inflammation of the kidney so you may pass less urine or have cloudy urine or bloody urine, swelling and low back pain
- Inflammation of the muscles so you may feel weak or pain in the muscles
- 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 the back, sick to your stomach, and vomiting that gets worse when you eat
- Inflammation of the eye so you may have redness of the eye, blurred vision, sensitive to light, have eye pain, see floaters or have headaches
- Dizziness or fainting (low blood pressure), flushing, rash, fever, shortness of breath or upset stomach at the time of receiving your infusion (IV) or just after, or pain at the site of infusion
- Inflammation of the pancreas (diabetes) so you may have too much sugar in your blood, may need to urinate more often, lose weight, feel thirsty, and may need regular insulin shots
- Inflammation of the nerves that may cause pain, weakness or tingling in the hands and feet, and may spread to the legs, arms and upper body leading to severe muscle weakness

Other Risks

Blood Collection and Intravenous (IV) catheter placement:

The risks of taking blood may include pain, redness, swelling and/or bruising where the needle enters your body, light-headedness and fainting. On rare occasions, local blood clot formation or infection with redness and irritation of the vein has occurred. The blood pressure cuff may cause discomfort or bruising to the upper arm. Approximately 8.5 mL of blood will be taken during your participation in this research study for research purposes only.

Electrocardiogram (ECG):

An ECG is an electrical tracing of your heart's activity. During the procedure, you will have electrodes (small sticky patches) placed on your chest skin and wires attached to them. There may be some pulling on your skin or irritation, similar to pulling off an adhesive bandage, when the patches are removed.

Tumor Biopsy:

As with any procedure, there are risks and discomforts. You may feel some amount of pain or discomfort during a biopsy, including slight, stinging pain when a local anesthetic is injected by needle to numb the area, pressure and dull pain where the biopsy needle is inserted, discomfort from lying still for an extended time, and soreness, inflammation, bleeding, swelling, and/or infection at the biopsy site. With a tumor biopsy, there is a rare possibility of tumor cells spreading into the nearby area. If a general anesthetic is used, you will not feel pain during the procedure because you will be asleep. Your physician will explain the details of the procedure and the risks to you, depending on how the biopsy will be obtained.

CT/PET scan:

You will be required to have CT and/or PET scans regularly to monitor the progress of your disease while you are in this study. These scans expose you to radiation; the amount depends on the number of body areas scanned. Too much radiation over time can lead to the development of second cancers or leukemia.

MRI:

There are no known risks or side effects with having an MRI. If a contrast material is used, your study doctor will tell you about possible side effects or allergic reaction.

Brain MRI scan:

You may not have an MRI done if you have metal in your body, for example, some hip replacements, hearing aids, pacemakers, bullets, or jewelry that cannot be removed. You should inform the technologist or physician if you have any metal in your body. During the MRI exam, you may feel some heat and hear tapping noises but have no reason to worry. Some people may have a 'closed in' feeling while inside the machine. The injection may make you sick to your stomach or have pain, warmth, swelling, bruising, a small blood clot or infection at the injection site. Rarely, you may get a rash or other signs of allergy from the injection or get a rare disease

where some of your body parts get scarred. If you have a history of kidney problems you must inform the technologist or physician as you may not be able to receive an injection during the MRI exam. Please talk to your physician if you have any concerns or questions.

Risks associated with gadolinium contrast:
You may have a small IV catheter placed before the MRI scan so that gadolinium contrast can be injected into a vein as this may help to better determine if your cancer has spread. With gadolinium contrast severe reactions are rare. The FDA approves the contrast agent Gadolinium for use with human participants. You need to know that there are certain risks associated with the use of that contrast. Some healthy subjects (fewer than 3%) may experience mild nausea, headache or dizziness after the injection. These side effects usually resolve without need for treatment. There is also a risk of allergic reaction (less than 1%). An allergic reaction can cause hives and itching or difficulty breathing. In individuals with kidney dysfunction, the gadolinium can cause a serious condition called nephrogenic systemic fibrosis. Because of this, prior to your MRI scan you will have to undergo blood work to make sure that your kidney function is normal.

Detailed information on the contrast agent Gadolinium can be provided to you at your request. You should inform your study doctor: (1) if you are pregnant or breast feeding, (2) if you have a history of allergic reactions to MRI or CT contrast agents, (3) if you have a history of kidney disease, seizure, asthma, or allergic respiratory disorders, and (4) if you have anemia or disease that affects red blood cells.

Bone scan:
A radioactive substance is injected into a vein in your arm. There is a slight risk of damage to cells or tissue from being exposed to any radiation, including the radiation released by the substance in this test. Side effects at the injection site may include pain, redness, swelling, and/or bruising where the needle enters the body. Some people can have allergic reactions to the substance put in their veins for this test. The allergic reactions can cause itching or rash. More serious allergic reactions can cause difficulty breathing, dangerously low blood pressure, or kidney damage.

Reproductive Risks:

Female:
It is not known if the study drug(s) may affect an unborn or nursing baby. If you are pregnant, trying to become pregnant or breast-feeding, you may not be in the study. The study doctor will perform a blood or urine pregnancy test before the start of and during the study, if you are able to have a baby.

If you are able to have a baby, you must avoid having sex (abstinence) or use reliable birth control methods during the study and for a period of 120 days after your last dose of

pembrolizumab. The following birth control methods are allowed during the study as per local regulations or guidelines:

Two (2) of the following barrier methods in combination:

- Diaphragm
- Condom
- Copper intrauterine device (IUD)
- Contraceptive sponge
- Spermicide

OR

One (1) of the above barrier methods in combination with:

- Hormonal contraceptives (including oral, subcutaneous, intrauterine, or intramuscular) that are registered and marketed containing estrogen and/or a progestational agent

If you become pregnant during the study you must notify the study doctor right away. The study drug will be stopped and you will be taken out of the study.

Male:

There may be risks if you are male and your partner is pregnant or trying to become pregnant. If you are male and your partner is able to have a baby, you and your partner must avoid having sex (abstinence) or use reliable birth control methods during the study and for a period of 120 days after your last dose of study drug pembrolizumab. The following birth control methods are allowed during the study:

Two (2) of the following barrier methods in combination:

- Diaphragm
- Condom
- Copper intrauterine device (IUD)
- Contraceptive sponge
- Spermicide

OR

One (1) of the above barrier methods in combination with:

- Hormonal contraceptives (including oral, subcutaneous, intrauterine, or intramuscular) that are registered and marketed containing estrogen and/or a progestational agent

If your partner becomes pregnant during the study you must notify the study doctor right away. If your partner is already pregnant when you begin the study you must use a condom (male) during the study and for a period of 120 days after your last dose of pembrolizumab. You must also agree to not donate sperm during the study and for a period of 120 days after your last dose of study drug.

If you or your partner become pregnant during the study, you may be asked permission to follow the outcome of the pregnancy and report the condition of your baby to the Sponsor. This would involve being contacted by study staff at least monthly to check on how you and your baby are doing until your pregnancy is over.

Benefits

If you agree to take part in this research study, we cannot guarantee that you will receive any benefits. We hope the information learned from this research study may benefit other patients with breast cancer in the future.

Economic Considerations

You will not be paid for taking part in this study. Tests and procedures that would be performed for your regular cancer care whether you are on this study or not are called "standard of care." All of the tests and procedures listed in this consent form that will be performed at your study visits are standard of care unless noted with an asterisk (*). There will be no charge to you or your insurance provider for the Pembrolizumab (MK-3475). The administration of the study drug, Pembrolizumab, will be charged to you or your insurance provider. There will be no charge to you or your insurance provider for tests or procedures noted with an asterisk as these are performed for study purposes only. All other tests and procedures will be charged to you or your insurance provider in the usual way as these are standard of care. This may include other tests and procedures not listed in this consent if your doctor feels it is necessary for your care, such as additional laboratory tests.

Taking part in this research study may lead to added costs for you or your insurance provider. You are encouraged to speak with your insurance provider prior to entering the research study to find out your individual coverage. If you have difficulty determining your individual insurance coverage, you may call Dr. Pusztai's office for assistance at 203-737-8309.

You or your insurance provider will be charged for continuing medical care and/or hospitalization that are not a part of the research study.

Treatment Alternatives

You do not have to participate in this study to be treated for your advanced cancer. Your other choices may include:

- Getting treatment with a marketed drug or care for your cancer without being in a study
- Taking part in another study.
- Receiving no 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.
  Comfort care does not treat the cancer directly but instead is meant 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.

Confidentiality and Authorization to collect, use and disclose Protected Health Information

For purposes of this study, Yale University, Yale-New Haven Hospital, and Dr. Pusztai will use medical information collected or created as part of the study, such as medical records and test results, which identifies you by name or in another way. Your consent to participate in the study means you agree that Yale University, Yale-New Haven Hospital, and Dr. Pusztai may obtain your medical information that they request for study purposes from your physicians and your other health care providers from the past or during your participation in the study.

The protected health information that will be collected in this study may include your name, address, phone number, medical history, photographs, date of birth, and information from your study visits. This health data may come from your family doctor or other health care workers.

Any identifiable information that is obtained in connection with this study will remain confidential and will be disclosed only with your permission or as permitted by U.S. or State law. Examples of information that we are legally required to disclose include abuse of a child or elderly person, or certain reportable diseases such as HIV or hepatitis. When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity unless your specific consent for this activity is obtained.

We understand that information about you obtained in connection with your health is personal, and we are committed to protecting the privacy of that information. If you decide to be in this study, the study staff will get information that identifies you and your protected health information. This may include information that might directly identify you, such as your name, date of birth, and medical record number**.** This information will be de-identified prior to providing it to the sponsor, meaning we will replace your identifying information with a code that does not directly identify you. The study doctor will keep a link that identifies you to your

coded information, and this link will be kept secure and available only to the Principal Investigator or selected members of the study team. Any information that can identify you will remain confidential.

The records for this trial will be stored in locked cabinets and/or offices and password protected computers. The study team will only give this coded information to others to carry out this research study or to sponsor representatives to comply with federal laws and regulations. It is anticipated that records containing the information that links you to your coded information will be maintained indefinitely, as there are no plans at this time to destroy these records at the end of the study.

Information about your study participation will be entered into your Electronic Medical Record (EMR). Once placed in your EMR, these results are accessible to all of your providers who participate in the EMR system. Information within your EMR may also be shared with others who are appropriate to have access to your EMR (e.g., health insurance company, disability provider.)

Information about you and your health which might identify you may be used by or given to:

- The U.S. Department of Health and Human Services (DHHS) agencies
- Representatives from Yale University and the Human Investigation Committee (the committee or Institutional Review Board that reviews, approves, and monitors research on human subjects), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential
- Your providers who are participants in the Electronic Medical Record (EMR) system
- Those individuals at Yale who are responsible for the financial oversight of research including billings and payments
- The study doctor, Dr. Lajos Pusztai, and the Yale study team
- The U.S. Food and Drug Administration (FDA). This is done so that the FDA can review information about the new drug product involved in this research. The information may also be used to meet the reporting requirements of drug regulatory agencies.
- The study sponsor or manufacturer of study drug, Merck and/ or their representatives
- Drug regulatory agencies in other countries
- Governmental agencies to whom certain diseases (reportable diseases) must be reported
- Health care providers who provide services to you in connection with this study.
- Laboratories and other individuals and organizations that analyze your health information in connection with this study, according to the study plan.
- Data and Safety Monitoring Boards and others authorized to monitor the conduct of the Study

In addition, the sponsor may provide access to clinical data that has been further de-identified so that outside researchers can use this data. Information that could directly identify you will not be included. Instead, it may include your initials, date of birth, and study visit dates.

The sponsor and those working for or with the sponsor, which may include affiliates of the sponsor, may use the health data sent to them:

- to see if the study drug works and is safe;
- to compare the study drug to other drugs;
- to develop new tests
- for other activities (such as development and regulatory) related to the study drug.

For these uses, the Sponsor may share this health data with others involved in these activities, as long as they agree to only use the health data as described here. The Sponsor and those working for or with the Sponsor, which may include affiliates of the Sponsor, may transfer health data about you from your country to other countries where the privacy laws are not as strict. Once the research team shares health data about you with others, it may no longer be protected by privacy laws.

There is a risk that if people other than the Sponsor, or those working for or with the Sponsor, may get your health data and genetic information. There is a risk that your information could be misused. The chance of this happening is very small. We have protections in place to lower this risk. There can also be a risk in uncovering genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a research study. Very rarely, health or genetic information could be misused by employers, health insurance companies, and others. There is a federal law called the Genetic Information Nondiscrimination Act (GINA) that, in general, makes it illegal for health insurance companies, group health plans, and most employers (except those with fewer than 15 employees) to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Your specimens and information will only be used for research and will not be sold. There is a possibility that this research may lead to development of products that will be commercialized. If this happens, there is no plan to share any financial gain with you or your family.

By signing this form, you authorize the use and/or disclosure of the information described above for this research study. The purpose for the uses and disclosures you are authorizing is to ensure that the information relating to this research is available to all parties who may need it for research purposes.

All health care providers subject to HIPAA (Health Insurance Portability and Accountability Act) are required to protect the privacy of your information. The research staff at Yale School of Medicine and Yale-New Haven Hospital is required to comply with HIPAA and to ensure the confidentiality of your information. Some of the individuals or agencies listed above may not be subject to HIPAA and therefore may not be required to provide the same type of confidentiality protection. They could use or disclose your information in ways not mentioned in this form. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

Authorized representatives of the Food and Drug Administration (FDA**)** and the manufacturer of the study drug being tested, Merck Sharp & Dohme Corp., may need to review records of individual subjects. As a result, they may see your name, but they are bound by rules of confidentiality not to reveal your identity to others.

The sponsor will see the research information we collect about you when they come to Yale to monitor the conduct of this research study. The "Sponsor" includes any persons that work for or are hired by the sponsor to conduct research activities related to this study. For this study the sponsor is Merck Sharp & Dohme Corp. Yale researchers will also send the sponsor your health information during the study or at the end of the study. When Yale researchers send information about you to the sponsor, they will not send information that directly identifies you such as your name.

You have the right to review and copy your health information in your medical record in accordance with institutional medical records policies. However, you will not be allowed to look at or copy your study related information until after the research is completed.

This authorization to use and disclose your health information collected during your participation in this study will never expire.

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

In Case of Injury

If you are injured while on study, seek treatment and contact the study doctor as soon as you are able. You can reach Dr. Pusztai's office by phone at 203-737-8309.

If you are injured as a direct result of the study drug or a properly performed procedure required by the study plan, the study sponsor will pay the reasonable costs of medical treatment. The study sponsor will not provide any other form of compensation. You are not being asked to release or waive any of your legal rights against the institution, the investigator or the sponsor for liability for negligence.

You will not receive any other kind of payment. There are no plans to pay you for such things as lost wages, disability, or discomfort as part of this study. You do not give up any of your legal rights by signing this consent form.

Voluntary Participation and Withdrawal

Participation in this study is voluntary. You are free to choose not to take part in this research study. Refusing to take part in this research study will not lead to penalty or loss of benefits to which you are otherwise entitled (such as your health care outside the study, the payment for your health care, and your health care benefits). However, you will not be able to enroll in this research study and will not receive study procedures as a study participant if you do not allow use of your information as part of this study.

Withdrawing From the Study:
If you decide to participate in this research study, you are free to stop and withdraw from this study at any time during its course. To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part. They will make sure that proper procedures are followed and a final visit is made for your safety. This will cancel any future research study appointments. If at some point you consider withdrawing from the study, you can decide if you are willing to continue to provide information or not. This would be helpful for the purposes of the study. To help you decide, the study doctor/staff can tell you which study procedures and information collection would still apply if you stop taking the study drug but choose to remain in the study.

The researchers may withdraw you from participating in the research if necessary.

Withdrawing from the study will involve no penalty or loss of benefits to which you are otherwise entitled. It will not harm your relationship with your own doctors or with Yale-New Haven Hospital. We would still treat you with standard therapy or, at your request, refer you to a clinic or doctor who can offer this treatment.

If you fail to give your consent by not signing this document, or if you cancel your consent later, then you will not be eligible to participate in this study and will not receive any treatment provided as part of the study. Unless and until you do cancel the consent, it will remain valid and effective.

Withdrawing Your Authorization to Use and Disclose Your Health Information:
You may withdraw or take away your permission to use and disclose your health information at any time. You do this by telling the study staff or by sending written notice to the study doctor, Dr. Pusztai, at the address listed on page one of this form. If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others until the end of the research study, as necessary to insure the integrity of the study and/or study oversight.

Questions

We have used some technical terms in this form. Please feel free to ask about anything you don't understand and to consider this research and the consent form carefully – as long as you feel is necessary – before you make a decision.

Authorization and Permission

I have read (or someone has read to me) this form and have decided to participate in the project as described above. Its general purposes, the particulars of my involvement and possible hazards and inconveniences have been explained to my satisfaction. I have had a chance to ask questions and they have been answered. My signature also indicates that I have received a copy of this consent form.

By signing this form, I give permission to the researchers to use and give out information about me for the purposes described in this form. By refusing to give permission, I understand that I will not be able to participate in this research.

I also confirm that I have received a Subject ID Card providing contact details of the study doctor and agree to carry this card with me at all times.

Study Participant (print name)	Signature	Date
Person obtaining consent (print name)	Signature	Date
Person obtaining consent (print name) – only if applicable, otherwise blank	Signature	Date
Interpreter/ Witness (print name) – only if applicable, otherwise blank	Signature	Date

If after you have signed this form you have any questions about your privacy rights, please contact the Yale Privacy Officer at (203) 432-5919.

If you have further questions about this project or if you have a research-related problem, you may contact the Principal Investigator, Dr. Lajos Pusztai, at 203-737-8309. If you would like to talk with someone other than the researchers to discuss problems, concerns, and questions you may have concerning this research, or to discuss your rights as a research subject, you may contact the Yale Human Investigation Committee at (203) 785-4688.