FOX CHASE CANCER CENTER
TEMPLE HEALTH

FOX CHASE CANCER CENTER
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**INFORMED CONSENT DOCUMENT**

# *A Phase I/II study to determine feasibility and safety of pembrolizumab (MK-3475) alone or in combination with copanlisib in relapsed or refractory NK and T-cell Non-Hodgkin lymphoma*

**Principal Investigator: Henry Fung, MD**

This is a clinical trial, a type of research study. Research studies are voluntary and include only people who choose to take part. Please read this consent form carefully and take your time making your decision. As your study doctor or study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. We encourage you to talk with your family, friends or family doctor before you decide to take part in this research study.

You are being asked to take part in this research study because you have relapsed or refractory NK and T-cell Non-Hodgkin lymphoma.

The sponsor-investigator of this study is Henry Fung, MD at Fox Chase Cancer Center. This study is supported by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc and Bayer.

## Why is this research study being done?

This is a research study to test an investigational drug, pembrolizumab, also known as MK-3475 alone or in combination with the investigational drug copanlisib for treatment of NK and T-cell Non-Hodgkin lymphoma.

Pembrolizumab is FDA approved for use in other cancers, such as melanoma, lung cancer and head and neck. Copanlisib is also FDA approved for use in Follicular Lymphoma (a type of cancer).

Your study doctor will discuss what drugs are approved and available as treatment for your cancer. The study doctor will discuss with you any reasons why you may not be allowed to take part in this research study.

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

## How many people will take part in this research study?

A total of around 48 people were to take part in this research study, 18 in Phase 1 (completed) and up to 30 in Phase 2.

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

### Before you begin the research study:

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

- Physical exam which will include height, weight and vital signs
- You will be asked questions about your medical history and daily activities
- You will be asked about the medicines you are taking or have recently taken (over-the-counter medications, supplements, prescription medications or illegal drugs)
- You will be asked about any side-effects you may be experiencing
- You will be asked to provide a tumor sample from a previous biopsy or surgical procedure if available. You will also be asked to provide a newly obtained tumor biopsy tissue sample
    - This sample will be tested to ensure it can be evaluated for the specific biomarkers to be tested in this study. Your sample 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
- Routine blood tests (about 1 tablespoon)
    - These samples will be used to check blood counts, kidney and liver function, thyroid function and the levels of certain enzymes and minerals normally found in the blood
- Blood (1 teaspoon) to test how fast your blood takes to clot
- A PET/CT scan or CT scan of your tumor
    - A PET scan requires an injection of a radioactive material into a vein and produces 3-D images to see how your cells work.
    - A CT scan is a computerized x-ray that gives your study doctor pictures of the inside of your body
    - A PET/CT scan combines the two scans to allow doctors to see the location and function of cells within the body
- Urine test
- Blood pregnancy test (1 teaspoon), if you are a female and able to become pregnant
- We will perform a blood test to check the presence of a viral infection (CMV)

### During the research study

#### Study Treatment

This study has two cohorts, cohort 1 and cohort 2. Patients in cohort 1 will be treated with pembrolizumab alone while patients in cohort 2 will be treated with the combination of

pembrolizumab and copanlisib. Cohort 1 is already completed and therefore you will be enrolled in cohort 2.

Cohort 2: This cohort has two phases of treatment, phase 1 and phase 2. In this cohort you will be asked to take Bactrim drug either one tablet daily (single strength) or three times a week (double strength) to prevent infections. This cohort has an induction phase prior to treatment cycles where patients will be infused with one of the drugs, copanlisib, twice- on day -21 and day -14 of 21 day period (called day -1 to -21 before treatment with the combination drugs) and blood will be collected prior to the first dose and a week after the second dose of the drug (day -21, prior to infusion, and day -7). After the 21 days long induction phase, treatment with combination of copanlisib and pembrolizumab will begin and administered in a cyclical manner.

Phase 1: Phase 1 portion is to determine the dose of copanlisib that is safe and tolerable in combination with pembrolizumab. If you are in this cohort, you will be administered a fixed dose of pembrolizumab (200 mg on day 1 of each cycle) and the dose of copanlisib will depend on the dose level at which you enter the study. It could either be 45 mg on day 1 or 45 mg on day 1 and day 8 or 60 mg on day 1 or day 8 of each cycle. Each cycle is 21 days long.

Phase 2: If you are enrolled in phase II portion you will be administered pembrolizumab 200 mg on day 1 of each cycle and copanlisib will be administered as determined to be safe and tolerable from phase 1 position. Each cycle is 21 days long.

**Tests and Procedures**

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

- Physical exam which will include weight and vital signs
- We will ask you about your ability to perform daily activities
- We will ask you about the medicines you are taking or have recently taken (over-the-counter medications, supplements, prescription medications or illegal drugs).
- We will ask you about all the side-effects that you may be experiencing
- Routine blood tests (about 1 tablespoon)
- Research blood tests (about 2-3 teaspoons)
    - These samples will be used to discover 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 studied
- A blood sample will be collected for genetic research
    - Your blood sample contains 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 blood may also be used to help develop new tests. The results are for research use only
- A PET/CT scan or CT scan of your tumor
- Blood test, once every cycle, to check the presence of a virus (CMV), only if the virus was detected in the test done at the time of the screening
- Blood will be collected (1 teaspoon) to test your thyroid function

**After you are finished with the study treatment**

Follow-up Visits:

- We will need to schedule a visit about 30 days after your last dose to see if you are experiencing any side effects from the treatment
- After the first follow up, you will continue to come in for a follow-up visits about every 12 weeks for up to two years or documentation of progression of your disease, whichever happens earlier, about every 26 weeks for the third year, and then about every 3 to 6 months for the rest of your life or until the study ends.
- If your cancer gets worse or you start a new treatment for your cancer, we would like to contact you by telephone about every 12 weeks for three years. After the third year, we would like to contact you about every 6 months.

Tests and Procedures

During the follow-up visits we would like to perform the following tests and procedures:

- We will ask you about all the side-effects that you may be experiencing
- Physical exam which will include weight and vital signs
- We will ask you about your ability to perform daily activities
- Routine blood tests (about 1 tablespoon)
- Research blood tests (about 2-3 teaspoons)
- Blood for (1 teaspoon) thyroid function test
- Tumor imaging – if you discontinued the study treatment for reasons other than worsening of your disease

**Study Chart**

You will receive Pembrolizumab and copanlisib every three weeks. This 3-week period of time is called a cycle. The cycle will be repeated until your disease gets worse. Each cycle is numbered in order. The chart below shows what will happen to you during Cycle 1 and future treatment cycles as explained previously. The left-hand column shows the day in the cycle and the right-hand column tells you what to do on that day.

| **Day** | **What you do…** |
|---|---|
| Before starting study | • Provide medical history<br>• Get a physical exam which will include height, weight and vital signs<br>• Report how you are performing your daily activities<br>• Provide all the side-effects you may be experiencing<br>• Report all medicines you are currently taking<br>• Get a routine blood test (1 tablespoon) |

| | |
|---|---|
| | • Blood test for minerals, liver and thyroid functions (1 tablespoon)<br>• Blood test for blood clotting (1 teaspoon)<br>• Blood test for CMV infection (1 teaspoon)<br>• Give a Urine sample<br>• Get a blood pregnancy test (1 teaspoon), if you are a female and able to become pregnant<br>• A PET/CT scan or CT scan of your tumor<br>• Collect a newly obtained biopsy sample, and if available, collect a cancer sample from a previous procedure (called “archival tumor tissue”). |
| Cycles 1 - 4 | • Report all medicines you are currently taking<br>• Get routine blood tests (1 tablespoon)<br>• Get research blood tests (about 2-3 teaspoons)<br>• Blood test for minerals, liver and thyroid functions (1 tablespoon)<br>• Blood test for CMV monitoring, if you were positive for CMV infection<br>• Report any side effects<br>• Get a physical exam which will include weight and vital signs<br>• Report how you are performing your daily activities<br>• Receive Pembrolizumab and copanlisib |
| Cycle 5 | • Get a physical exam which will include weight and vital signs<br>• Report how you are performing your daily activities<br>• Report any side effects<br>• Get a PET/CT scan or CT scan of your tumor<br>• Blood test for Liver and thyroid functions<br>• CMV monitoring<br>• Report all medicines you are currently taking<br>• Get routine blood tests (1 tablespoon)<br>• Receive Pembrolizumab and copanlisib |

**Future cycles**

| **Day** | **What you do…** |
|---|---|
| Future Treatments Up to Cycle 36 | • Get a physical exam which will include weight and vital signs<br>• Report any side effects<br>• Report all medicines you are currently taking<br>• Report side-effects you may be experiencing<br>• Report how you are performing your daily activities<br>• CMV monitoring<br>• Blood test for liver and thyroid functions<br>• Get routine blood tests (1 tablespoon)<br>• Get a PET/CT scan or CT scan of your tumor (every 12 weeks)<br>• Receive Pembrolizumab and copanlisb |
| End of Treatment | • Report all medicines you are currently taking<br>• Report any side effects you may be experiencing<br>• Report how you are performing your daily activities<br>• Get a physical exam which will include weight and vital signs<br>• Get routine blood tests (1 tablespoon)<br>• Get your thyroid function test |

| | |
|---|---|
| | • Get a PET/CT scan or CT scan of your tumor |

**How long will you be in the research study?**

You may receive treatment with pembrolizumab and copanlisib for up to 2 years or until your disease gets worse, whichever happens earlier**.**

**Can you stop being in the research study?**

Yes. Your participation in this research is completely voluntary. If you agree to participate now and change your mind later, you may withdraw at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely and will discuss with you options for withdrawal such as continuing to provide further data collection from routine medical care.

**Can you be removed from this research study?**

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

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

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

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

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

**Very Common (≥ 10%)**

- Fatigue – feeling tired
- Decreased hunger
- Cough
- Pruritus- itching of the skin
- Diarrhea- loose or watery stool
- Rash
- Nausea
- Shortness of breath
- Joint pain
- Constipation
- Headache
- Vomiting

- Asthenia- abnormal physical weakness or lack of energy
- Fever
- Back pain
- Anemia- lack of red blood cells resulting in pale color and weakness
- Peripheral edema- swelling or puffiness in the body due to too much liquid accumulation in body's tissues, especially, lower limbs
-

**Common (1% to 10%)**

- Pneumonia- infection of the lungs in which your lungs get filled with fluid leading to shortness of breath and cough with phlegm or pus, fever, chills. Sometimes this might lead to death
- Hyperthyroidism- too much thyroid hormone so you may feel anxious, angry, can't sleep, weak, tremble, increased sweating, weight loss, hair loss, tired, have diarrhea
- Hypothyroidism- not enough thyroid hormone so you may feel tired, gain wright, feel cold, have infrequent or hard stools
- Pleural effusion- water in the lungs that may lead to cough, sharp chest pain, or shortness of breath
- Pneumonitis- inflammation of lungs, symptoms may include shortness of breath, cough, fatigue, loss of appetite and unintentional weight loss
- Colitis- chronic digestive disease of inflammation of the bowels/ gut, which may cause severe pain in your belly with loose or water stools, and black, tarry, sticky stools or stools with blood or mucus, loss of appetite
- Pulmonary embolism- sudden chest pain and shortness of breath

**Uncommon (0.1 to < 1%)**

- Infusion related reaction (drug hypersensitivity, anaphylactic reaction, hypersensitivity and cytokine release syndrome)- allergic reaction to infusion where you may feel dizzy or faint, flushed, get a rash, have a fever, feel short of breath at the time of receiving your infusion (IV) or just after, or pain at the site of infusion of the drug
- Change in taste
- Dehydration
- Pain in your belly
- Acute kidney injury- sudden kidney failure
- Skin cancer
- Chronic obstructive pulmonary disease (COPD)- symptoms may include shortness of breath, wheezing, or a chronic cough
- Pericardial effusion- accumulation of water around heart
- Cellulitis- a painful bacterial skin infection
- Kidney failure
- Urinary tract infection- it may cause pelvic pain, increased urge to urinate, pain with urination, and blood in the urine
- Respiratory failure

- Sepsis- this is caused by body's over-reaction to infection, symptoms may include fever, difficulty in breathing, low blood pressure, fast heart rate and mental confusion
- Irregular heartbeat
- Hypophysitis- 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, extreme thirst
- Adrenal insufficiency- Adrenal glands (glands on top of the kidneys) that may not make enough hormone, which could cause tiredness, weight loss, muscle weakness, feeling faint, joint, muscle and belly aches, nausea, vomiting, loose or watery tools, fever, salt craving, and sometimes darkening of the skin like a suntan
- Type 1 diabetes mellitus (diabetic ketoacidosis)- 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, a diabetic complication where body produces too much acid
- Hyponatremia- low level of sodium in the body, symptoms may include nausea, headache, confusion and fatigue, restlessness and irritability, muscle weakness or spasms, seizure, coma
- Uveitis (iritis, iridocyclitis)- inflammation of the eye so you may have blurred vision, sensitivity to light, eye pain, see floaters or have headaches
- Myositis- inflammation of the muscles so you may feel weak or have pain in your muscles
- Myocarditis- 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. Sometimes this condition can lead to death
- Pancreatitis- inflammation of the pancreas (a gland in your abdomen that controls sugar level) so you may have severe pain in the top part of your belly that may move to your back, feel sick to your stomach, and vomiting that gets worse when you eat
- Hepatitis- inflammation of the liver that may make you feel sick to the stomach and vomit, feel like not eating, feel tired, have a mild fever, have pain in the right side of the belly, yellow eyes and skin, and dark urine
- Nephritis- inflammation of the kidney so you may pass less urine or have cloudy or bloody urine, swelling in the face, legs and feet, and lower back pain

**Rare (0.01% to 0.1%)**

- Thyroiditis- inflammation of the thyroid gland, an organ that makes and stores thyroid hormones. This condition may lead to change in your heart rate, body temperature, and the rate at which food is converted into energy, sensitivity to cold, puffy face, dry hair, dry skin, weight gain or loss, fatigue, diarrhea or constipation
- Severe skin reactions- 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. These severe conditions can sometimes lead to death

- Guillain-Barre Syndrome- an autoimmune condition where your immune system attacks your nerves that may cause severe lower back pain, muscle weakness in your legs that travels to your upper body, prickling or tingling sensation in your fingers and toes, paralysis, loss of bladder control, difficulty moving your eyes or face, talking, chewing or swallowing, fast heart rate, difficulty breathing
- Myasthenic syndrome- a condition that may make you feel weak and tired and might have drooping of the eyelids, blurred or double vision, difficulty swallowing, slurred speech, weakness in your arms and legs, or difficulty breathing
- Sarcoidosis- the formation of small clusters of immune cells (called granulomas) in parts of your body, such as, your lymph nodes, eyes, skin or lungs, symptoms vary depending on the organ affected and includes shortness of breath, cough that won't go away, reddish bumps on the skin, fever, fatigue, night sweats, weight loss
- Encephalitis- 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
- Toxic epidermal necrolysis- a disorder of skin and outer lining that may cause a painful, red are that spreads quickly, skin may peel without blistering, raw areas of skin, discomfort, condition may spread to eyes, mouth/throat, and genitals/ urethra/ anus
- Stevens-Johnson syndrome- a disorder of the skin and outer lining that may begin with flu like symptoms, a painful rash that spreads and blisters follow, peeling of the skin, rash of small purplish spots, red spots or bumps, fever, malaise, eye redness, coughing, itching, mouth ulcers, sensitivity to light, sore throat or swelling

**Other events that may occur but can not be estimated from the available data**

- Solid organ transplant rejection

Patients treated with pembrolizumab who then go on to allogeneic stem cell transplant (a procedure in which a person receives blood-forming stem cells from a donor), should inform their transplant physician that they may have received pembrolizumab in the past.

In patients with any hematologic malignancy (cancers 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.

Reports of clotting of blood within the liver and severe graft versus host disease (which may include skin, liver and gastrointestinal symptoms), including death, have been received for patients who received allogeneic stem cell transplant after pembrolizumab therapy.

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

**Very Common (≥ 10%)**

- Decrease in white blood cells (leukopenia) which can interfere with the ability to fight infections
- Decreased hemoglobin [anemia, hemoglobin decreased] leading to tiredness and pale skin, and may become life-threatening
- Raised blood sugar levels [hyperglycemia]. In some instances this may be severe and life-threatening

- Raised blood pressure [hypertension including hypertensive emergency]
- Feeling tired [fatigue and asthenia]
- Nausea
- Diarrhea
- Inflammation of the mouth and lips (stomatitis) with or without oral ulceration and oral pain
- Rash
- Low phosphate levels in the blood (hypophosphatemia) that can cause muscle weakness, respiratory failure and heart failure, seizures and coma
- Decreased number of a type of white blood cells called neutrophils [neutropenia]. This may occur with other signs of infection and may become life-threatening [neutropenia]
- Decreased number of a component of blood called platelets that help with the formation of blood clots [thrombocytopenia, platelet count decreased].
- Lower respiratory tract infections (including pneumonia, pneumonia due to bacteria, virus or a fungal infection). Such infections may be severe and have life threatening or fatal outcome.

**Common (≥ 1% to < 10 %):**

- Low levels of a type of blood cells called lymphocytes (lymphopenia) causing weakness, tired, weight loss, chills, fever, night sweats, pain or feeling of fullness in the belly
- Change in your sense of taste (dysgeusia)
- High level of disease-fighting white blood cells known as eosinophils in the blood (eosinophilia) that can cause allergies, asthma, inflammatory conditions in the stomach and skin, such as, eczema
- Febrile neutropenia- development of fever with infection due to low number of a cell type in the blood (neutrophils) that can be life threatening
- Dry mouth
- Difficulty swallowing (Dysphagia)
- Swelling in the lining of intestines (mucosal inflammation)
- Injection site reactions
- Hypersensitivity reactions (including allergic swelling of the skin (edema and angioedema), widening of blood vessels and flushing, and infusion related reaction)
- High levels of enzymes lipase and amylase that can cause severe abdominal pain, fever, loss of appetite, nausea, vomiting, yellowing of eyes
- High lipids, such as cholesterol and triglycerides (hyperlipidemia)
- High levels of insulin in the blood (hyperinsulinaemia) causing weight gain, craving or sugar, intense hunger at higher frequency, feeling anxious, fatigue and lacking focus
- Abnormal feeling of constant thirst (polydipsia paresthesia)
- Unpleasant, abnormal sense of touch often present as pain or an inappropriate but not discomforting sensation (dysesthesia)
- Pneumonitis (including interstitial lung disease and noninfectious pneumonitis)
- Sudden hair loss that starts with one or more circular bald patched (alopecia)

**Uncommon (≥0.001% to <1%)**

- Swelling of the pancreas (pancreatitis)

It is possible that if your blood sugar increases (hyperglycemia), glucose lowering medications (insulin and/or an oral medication) or even hospitalization may be required.

If you experience respiratory symptoms such as cough, shortness of breath, or fever, it may be caused by pneumonitis or respiratory infections (such as pneumonia or lung infections) in some cases. These conditions usually respond well to therapy, but may become life-threatening or fatal if not promptly treated. Please contact your doctor for further advice if you experience any of these symptoms.

**Opportunistic Infections:**
During treatment with copanlisib you may develop bacterial or viral infection. In order to prevent developing of such infections additional tests will be performed on a regular basis. Your physician may advise using prophylactic treatment for this kind of infection at any time during treatment with copanlisib.

As the study drug is under development, there may be side effects, including allergies that are not yet known. Therefore, you must notify your study doctor of any new symptoms that you may have whether or not you think they are caused by the study drug.

You may experience some of these side effects, which are usually temporary and manageable. However, this study may include risks that are yet unknown and may cause serious problems or even death.

**Radiation Risk for Diagnostic Imaging**

- It is unlikely that there will be any harmful effects from the radiation exposure you will receive from participating in this study
- At high levels of exposure, scientists agree that radiation can cause cancer
- At low exposure levels most scientists agree that the risk, if any, is very low. You will have low levels of radiation exposure with diagnostic imaging procedures
- Risks from exposure to radiation may accumulate over a lifetime
- CT Scan: CT scans are used to create images of internal bones and organs using radiation
    - High dose radiation is known to produce cancer cells. The effect of exposure to radiation adds up over a lifetime
    - The amount of radiation exposure involved in this trial will not be significantly greater than for subjects with your disease who do not take part in the trial.
    - The contrast solution that may be given for a CT scan may cause an allergic reaction (rare)
        - Severe allergic reactions can be life threatening
        - CT contrast solution can cause kidney damage, especially if you are diabetic, dehydrated (lost body water) or elderly

**Blood Draw Risks**

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

**IV line Risks**

- Discomfort
- Irritation
- Mild bruising
- Bleeding
- Leakage of drug solution, and rarely, infection, nausea, and lightheadedness.

**Biopsy Risks**

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

Other less common side effects have been reported with the use of the drugs in this study. The study doctor or staff can discuss these with you. There may also be other side effects or risks that are not known at this time.

**Reproductive Risks**

- Study treatments may make you sterile (unable to have children)
- The drugs in this study may affect a baby, before or after the baby is born
- If you are pregnant now or if you are breast-feeding now, you may not take part in this research study
- If you become pregnant while you are on the research study, you must notify the study doctor right away. The study drug will be stopped and you may not continue to take part in the research study

**For women who can become pregnant:**

- You should not become pregnant while you are in this study and up to 120 days after the last dose of study therapy
- You should not breast-feed your baby while taking drugs for this research study
- The study doctor will perform blood pregnancy tests before the start of and during the study, if you are able to have a baby

**For men:**

- You should not make a woman pregnant while you are in this study and up to 120 days after the last dose of study therapy

**For women and men:**

- If you are having sex that could lead to pregnancy, you should use birth control while you are in this study
- Check with the study doctor about birth control methods and how long to use them. 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

**OR**

**Abstinence is acceptable if this is your established and preferred contraception**

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.

**Genetic Information Nondiscrimination Act (GINA)**

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

## Are there benefits to taking part in the study?

Taking part in this study may or may not make your health better. While doctors hope the treatment will be more useful against cancer compared to the usual treatment, there is no proof of this yet. We do know that the information from this study will help doctors learn more about pembrolizumab and copanlisib as a treatment for cancer. This information could help future cancer patients. The sponsor does not intend to provide you with ownership or financial benefits that may result from this study.

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

Your other choices may include:

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

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

## Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

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

- Fox Chase Cancer Center and affiliated Joint Centers, The Institutional Review Boards of The Fox Chase Cancer Center and Temple University, Temple University, Temple University Health system, Inc., and its affiliates or subsidiaries and other authorized representatives of these organizations.
- Merck Sharp & Dohme Corp., (a subsidiary of Merck & Co. Inc.)
- Bayer
- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people
- Study team members at collaborating sites

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

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

## What are the costs?

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

Merck will supply pembrolizumab and Bayer will supply copanlisib at no charge while you take part in this study. However, the cost of getting the pembrolizumab and copanlisib ready and giving it to you will not be covered, so you or your insurance company may have to pay for this.

Study related tests will be provided at no cost to you.

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

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

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

## Will you be compensated?

You will not get paid for taking part in this research study.

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

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

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

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

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

## New findings

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

## Who can answer your questions about the research study?

| If you have questions about: | Please Call: |
|---|---|
| This study, including if you get sick or hurt | Dr. Fung at 215-728-4300 |
| If you have a concern or complaint | Risk Management Department at 215-728-2591 |
| Your rights as a research participant on this study | FCCC Institutional Review Board at 215-214-3754 |
| Your bills or health insurance coverage | Clinical Trial Financial Counselor at 215-214-3768 |

## Where can you get more information?

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

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

- You may also visit the NCI website at http://cancer.gov
- For NCI's clinical trials information, go to: http://cancer.govclinicaltrials/
- For NCI's general information about cancer, go to: http://cancer.gov/cancerinfo/

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

| | | |
|---|---|---|
| **Signature of Participant** | **Print Name of Participant** | **Date** |

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

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

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

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