UNIVERSITY OF CALIFORNIA LOS ANGELES
ADDENDUM CONSENT
ADDITIONAL INFORMATION FOR CONTINUING RESEARCH PARTICIPANTS

Phase II study of an Investigational Drug in Patients with Non-Small Cell Lung Cancer (NSCLC)

Phase II study of pembrolizumab in EGFR mutant, tyrosine kinase inhibitor naïve treatment patients with advanced non-small cell lung cancer (NSCLC)

Dr. Edward B. Garon, and associates from the Division of Hematology-Oncology at the University of California, Los Angeles are conducting a research study.

You are participating in the above named research study. When you agreed to participate, the researchers told you they would share any new information about the study that might affect your willingness to continue to participate in the study.

The study now involves new risk information that are described below. The researchers will explain the new risk information and then ask for your consent [to continue participating in the study.

WHAT ARE THE NEW PROCEDURES INVOLVED IN THIS STUDY?

We have learned of new information since you began participating in this research. If the new information involves a change in the risks or alternatives, an investigator will review this information with you in detail.

WHAT KINDS OF RISKS OR DISCOMFORTS COULD I EXPECT?

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 that may become serious or life-threatening, and in some cases, may lead to death.

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

VERY COMMON, SOME MAY BE SERIOUS (i.e. causing hospitalization, life-threatening or where noted, may cause death) Out of 100 people who receive pembrolizumab, 20 or more people may have the following:

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

COMMON, SOME MAY BE SERIOUS (i.e. causing hospitalization, life-threatening, or where noted, may cause death) Out of 100 people who receive pembrolizumab, at least 5 but less than 20 people may have the following:

- Joint Pain
- Fever
- Back pain
- Rash
- 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
- 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

UNCOMMON, SOME MAY BE SERIOUS (i.e. causing hospitalization, life-threatening, or where noted, may cause death)

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

- Too much thyroid hormone so you may feel anxious, angry, have trouble sleeping, feel weak, tremble, sweat, feel tired, have loose and watery stools
- Inflammation of the lungs so you may feel short of breath and cough. Sometimes this might lead to death.
- Inflammation of the bowels/gut, which may cause pain in your belly with loose or watery stools, and black, tarry, sticky stools or stools with blood or mucus
- 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.
- Infusion reaction, 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

RARE, SOME MAY BE SERIOUS (i.e. causing hospitalization, life-threatening, or where noted, may cause death)
Out of 100 people who receive pembrolizumab, less than 1 person may have the following:

- 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.

- 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.

- 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 abdominal aches, nausea, vomiting, loose or watery stools, fever, salt craving and sometimes darkening of the skin like a suntan.

- Inflammation of the kidney so you may pass less urine or have cloudy 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 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.

- Inflammation of the eye so you may have eye redness, blurred vision, sensitivity to light, eye pain, see floaters or have headaches.

- 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 nerves that may cause pain, weakness or tingling in your hands and feet, and may spread to your legs, arms and upper body leading to severe muscle weakness and possible temporary paralysis.

- 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.

- 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.

- 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

- The formation of small clusters of immune cells (called granulomas) in parts of your body such as your lymph nodes, eyes, skin, or lungs

- 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

In addition to the above, **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 may lead to death.

Additional serious side effects seen in <1.0% of patients treated with pembrolizumab/KEYTRUDA® include the following:
Dizziness or fainting (low blood pressure), flushing, rash, fever, shortness of breath or sick to your stomach at the time of receiving your infusion (IV) or just after, or pain at the site of infusion.

In addition to the above, the following side effect(s) have been seen in patients on pembrolizumab, but are still being evaluated to determine if they are related to the drug:
A condition where you will feel weakness and fatigue of your hip and thigh muscles and an aching back caused by your body's immune system attacking your healthy cells and tissues.

Unknown risks and discomforts of the study drug
The experimental drug may have side effects that no one knows about yet. In addition, it is unknown whether initiating pembrolizumab prior to other therapies may have either a positive or a negative effect on subsequent therapies.

One patient died of inflammation of the lungs while receiving subsequent therapy with the EGFR inhibitor erlotinib. The possibility of a potential relationship to the prior pembrolizumab is unknown.

The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

WHAT OTHER CHOICES DO I HAVE IF I DON'T WANT TO PARTICIPATE?

You may wish to talk with your treating physician about your choices before deciding if you will take part in this study.

If you decide not to participate in this study, your other choices may include:

- Receiving an EGFR tyrosine kinase inhibitor (TK) such as gefitinib, erlotinib, or afatinib. These drugs are associated with a response rate (significant tumor shrinkage) of up to 70%.
- Receiving chemotherapy. Although reports vary, the response rate for chemotherapy would be expected to be approximately 35%.
- Receiving no treatment at this time.
- Taking part in another study.
- Receiving comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems, and other problems caused by your disease. It does not treat the diseases directly, but instead tried to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

We do not anticipate that we will see this high of a response rate in EGFR mutant patients treated with frontline pembrolizumab as is seen with EGFR TKIs. However, the researchers conducting this study are evaluating whether treating with pembrolizumab prior to an EGFR TKI will be a better overall strategy for the management of disease of the entire course of a patient's treatment.

Talk to your doctor about your choices before you decide whether you will take part in this study. If you choose not to participate in this study, it will not affect the other options available to you.

During the course of the study, you will be informed of any significant new findings (either good or bad), such as changes in the risks or benefits resulting from participation in the research or new alternatives to participation, that might cause you to change your mind about continuing in the study. If new information is provided to you, your consent to continue participating in this study will be re-obtained.

WHAT ARE MY RIGHTS IF I DECIDE TO CONTINUE TO TAKE PART IN THIS STUDY?

Continuing to take part in this study is your choice. You can choose whether or not you want to continue to participate. Whatever decision you make, there will be no penalty to you and you will not lose any of your regular benefits.

- You have a right to have all of your questions answered before deciding whether to take part.

- Your decision will not affect the medical care you receive from UCLA.
- If you decide to continue to take part, you can leave the study at anytime.
- If you decide to stop being in this study you should notify the research team right away. The researchers may ask you to complete some procedures in order to protect your safety.
- If you decide not to take part, you can still get medical care from UCLA.

WHO CAN I CONTACT IF I HAVE QUESTIONS ABOUT CONTINUING IN THIS STUDY?

The Research Team:
You may contact the investigators below with any questions or concerns about the research or your participation in this study. You can also call the UCLA Page Operator at (310) 825-6301 to reach any of the investigators below 24 hours a day, 7 days a week.

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UCLA Office of the Human Research Protection Program (OHRPP):
If you have questions about your rights while taking part in this study, or you have concerns or suggestions and you want to talk to someone other than the researchers about the study, you may contact the UCLA OHRPP by phone: (310) 825-5344; by email: mirb@research.ucla.edu or U.S. mail: UCLA OHRPP, 10889 Wilshire Blvd., Suite 830, Los Angeles, CA 90095.

Public Information about this Study:
ClinicalTrials.gov is a website that provides information about federally and privately supported clinical trials. A description of this clinical trial will be available on

http://www.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.

HOW DO I INDICATE MY AGREEMENT TO PARTICIPATE?

If you want to continue to participate in this study you should sign and date below. You have been given a copy of this consent form and the Research Participant's Bill of Rights to keep. You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

SIGNATURE OF THE PARTICIPANT

_____
Name of Participant

_____ _____
Signature of Participant Date and Time

SIGNATURE OF PERSON OBTAINING CONSENT

_____ _____
Name of Person Obtaining Consent Contact Number

_____ _____
Signature of Person Obtaining Consent Date and Time