Protocol Plain Language Summary

Study of pembrolizumab plus hyaluronidase with chemotherapy compared to pembrolizumab with chemotherapy in people with lung cancer (MK-3475A-D77)

Protocol title: A Phase 3 Randomized, Open-label Clinical Study to Evaluate the Pharmacokinetics and Safety of Subcutaneous Pembrolizumab Coformulated With Hyaluronidase (MK-3475A) Versus Intravenous Pembrolizumab, Administered With Chemotherapy, in the First-line Treatment of Participants With Metastatic Non-small Cell Lung Cancer

Why is this study needed?

Researchers are looking for new ways to treat people with **non-small cell lung cancer** (**NSCLC**) that has spread to other parts of the body (**metastatic**). NSCLC is one of the 2 major types of lung cancer.

Pembrolizumab is an **immunotherapy**, which is a treatment that helps the immune system fight cancer. Pembrolizumab is currently given through a needle in a vein as an intravenous (IV) infusion (**IV pembrolizumab**). Giving pembrolizumab as an injection under the skin (subcutaneous or SC injection) may make it easier to give and more convenient for people compared to an IV. An SC injection of pembrolizumab (**SC pembrolizumab**) also contains **hyaluronidase,** which helps pembrolizumab easily move into and through the body.

In this study, researchers want to learn if SC pembrolizumab reaches the same levels in a person's body over time compared to IV pembrolizumab (pharmacokinetics or PK study).

Who will take part in this study?

About 339 people with metastatic NSCLC will be in this study. They will be ages 18 years and older and should not have received any prior treatment for NSCLC, except for radiation.

How is this study designed?

People may be in this study for up to 5 years.

People will receive SC pembrolizumab and chemotherapy or IV pembrolizumab and chemotherapy. Both the people in the study and the researcher will know which study treatment a person is getting (an open-label study).

People may give urine samples, have blood, tumor, and imaging tests, have physical examinations, and answer sets of questions during the time they are in the study.

What treatments are being studied?

People will be assigned by chance to receive pembrolizumab in one of these ways:

- **SC pembrolizumab** (pembrolizumab and hyaluronidase) given as an SC injection
- **IV pembrolizumab** given as an IV infusion

People will receive pembrolizumab for about 25 months.

All people in the study will get **chemotherapy as an IV infusion**. The researcher will choose the type of chemotherapy and when it is given based on the type of NSCLC.

What are the goals of this study and how will they be measured?

Main goal	How it will be measured
To compare what happens to **pembrolizumab** in a person's body over time after it is given SC or IV	Blood samples are taken at different time points during the study to measure the: • total amount of pembrolizumab over time measured after the first dose • lowest amount of pembrolizumab needed for treatment measured at steady state; Steady state is when the amount remains the same over time after multiple doses.
Other goals	**How they will be measured**
To learn what happens to pembrolizumab in a person's body over time after it is given SC or IV	Blood samples are taken at different time points from before the first treatment and up to Week 6 of the third cycle to measure the: • total amount of pembrolizumab over time measured at steady state • highest amount of pembrolizumab measured after the first dose and measured at steady state • lowest amount of pembrolizumab needed for treatment measured after the first dose
To learn if a person's immune system makes **antibodies** against pembrolizumab after it is given SC or IV	The number of people who have a positive test for antibodies against pembrolizumab
To learn how many people who receive SC compared to IV pembrolizumab have the **cancer respond**	Researchers will measure responses throughout the study: • **objective response rate**: the percent of people with cancer that responds to treatment • **progression-free survival**: the average length of time after the start of treatment, that people are alive, and the cancer does not grow or spread • **overall survival**: the average length of time that people live from the start of treatment to death from any cause • **duration** of **response**: the average length of time from when the cancer first responds to treatment until the cancer gets worse or death from any cause
To learn about the safety and how well people manage (tolerate) the study treatments	The number of people who: • Had an adverse event (AE) during the study. An AE is any health problem that happens during a study • Stopped treatment during the study due to an AE
To learn how SC pembrolizumab affects people's **quality of life** compared to IV pembrolizumab	Researchers will compare people's answers to questions about their health and their ability to carry out daily tasks from when they start the study until the end of the study

What are the possible benefits and risks?

People in this study may or may not have their cancer stop growing or go away. This study has a Data Monitoring Committee that oversees the study's overall risk and benefit. If this committee decides that the study treatment is not safe or does not show benefit, the study can be stopped.

More information about the benefits and risks is in the Investigator Brochure, Protocol, and Informed Consent documents.