Protocol Plain Language Summary

A clinical study of MK-1084 and pembrolizumab to treat lung cancer (MK-1084-004)

Protocol Title: A Phase 3, Randomized, Double-blind, Multicenter Study of MK-1084 in Combination With Pembrolizumab Compared With Pembrolizumab Plus Placebo as Firstline Treatment of Participants With KRAS G12C-Mutant, Metastatic NSCLC With PD-L1 TPS ≥50%

Why is this study needed?

Researchers are looking for other ways to treat **metastatic non-small cell lung cancer (NSCLC)** with tumors that have a gene mutation called KRAS G12C. **Metastatic** means the cancer has spread to other parts of the body. A **gene mutation** is a change in the order of DNA.

A standard treatment for metastatic NSCLC is an immunotherapy, such as **pembrolizumab**. **Immunotherapy** is a treatment that helps the immune system fight cancer. **MK-1084**, the study medicine, is a targeted therapy for the KRAS G12C mutation. A **targeted therapy** is a treatment that works to control how specific types of cancer cells grow and spread.

The goal of this study is to learn if people who receive MK-1084 and pembrolizumab live longer overall and without the cancer getting worse compared to people who receive placebo and pembrolizumab. A **placebo** looks like the study medicine but has no study medicine in it. Using a placebo helps researchers better understand the effects of the study medicine.

Who will take part in this study?

About 600 people will be in this study. They will be at least 18 years old and:

- Have newly diagnosed metastatic NSCLC
- Have provided a tumor tissue sample that has:
  - The KRAS G12C mutation
  - PD-L1 in at least half of the tumor cells. **PD-L1** is a type of protein found on cancer cells that can help the cancer hide from the body's immune system.
- Have not had certain treatments for metastatic NSCLC in the past 6 months

What treatments are being given during the study?

People will have an equal chance to receive one of these treatments:

- **MK-1084** and **pembrolizumab**
- **Placebo** and **pembrolizumab**

People will take MK-1084 or placebo every day by mouth as a tablet until the cancer gets worse or the person doesn't tolerate it.

People will also receive pembrolizumab once every 3 weeks through a needle into a vein as an intravenous (IV) infusion. They will receive pembrolizumab for up to 2 years unless the cancer gets worse or the person doesn't tolerate it.

How is this study designed?

Neither the people in the study nor the researchers will know which treatment a person is taking (double-blind study). During the study, people will give blood and tumor tissue samples, have imaging tests and physical examinations, and answer questions about how they are feeling and their ability to carry out daily tasks.

A person may be in this study for about 4 and a half years.

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

Main goals	How they will be measured
To learn if the **progression-free survival (PFS)** of people who receive MK-1084 and pembrolizumab is longer than those who receive placebo and pembrolizumab	**PFS** is the length of time from when the person starts the study until the cancer grows or spreads, or death from any cause.
To learn if the **overall survival (OS)** of people who receive MK-1084 and pembrolizumab is longer than those who receive placebo and pembrolizumab	**OS** is the length of time from when the person starts the study until death from any cause.

Other goals	How they will be measured
To compare the **cancer response** in people who receive MK-1084 and pembrolizumab to those who receive placebo and pembrolizumab	During the study, researchers will measure: • **Objective response rate (ORR)**: the number of people whose cancer responds to treatment (gets smaller or goes away) • **Duration of response (DOR)**: the length of time from when the cancer first responds to treatment until the cancer grows, spreads, or death from any cause
To learn about the **safety** and how well people **tolerate** MK-1084 and pembrolizumab	The number of people who: • Have an **adverse event (AE)** – An AE is a health problem that happens or worsens during a study • Stop treatment due to an AE
To compare the **quality of life (QoL)** of people who receive MK-1084 and pembrolizumab to those who receive placebo and pembrolizumab	People will answer sets of questions to measure their **QoL**, including questions about their overall health, lung cancer symptoms, and their ability to carry out daily tasks. Researchers will measure: • The change in the scores during the study • The length of time from when the person starts the study until their QoL gets worse

What are the possible benefits and risks?

People may or may not benefit from the treatment received during the study. This study has an external group of experts who oversee the overall risk and benefit. If this group of experts 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 protocol.