Protocol Plain Language Summary

A clinical study of study medicines with or without pembrolizumab in people with melanoma that has spread to the brain (MK-3475-02D)

Protocol Title: A Phase 1/2 Open-Label Rolling-Arm Umbrella Platform Design of Investigational Agents With or Without Pembrolizumab or Pembrolizumab Alone in Participants With Melanoma (KEYMAKER-U02): Substudy 02D

Why is this study needed?

Researchers are looking for better ways to treat people with metastatic **melanoma**. **Melanoma** is a type of skin cancer. **Metastatic** means cancer has spread to other parts of the body.

Researchers want to learn if the **study medicines pembrolizumab, quavonlimab, and lenvatinib** can treat melanoma. Pembrolizumab and quavonlimab are immunotherapies. **Immunotherapy** is a treatment that helps the immune system fight cancer. Lenvatinib is a targeted therapy. 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 about the safety of the study medicines and the number of people whose cancer responds to treatment (the cancer gets smaller or goes away).

Who will take part in this study?

About 50 to 100 people with melanoma will be in each group of this study. They will be ages 18 years and older and have:

- Melanoma that has spread to the brain (called **brain metastasis**)
- Not had radiation therapy within 2 weeks of starting study treatment. **Radiation therapy** is a treatment that uses beams of intense energy (similar to X-rays) to shrink or get rid of tumors.

What treatments are being given during the study?

People will be assigned to groups to receive one or more of these:

- **Pembrolizumab**
- **Quavonlimab**
- **Lenvatinib**

People will receive pembrolizumab and quavonlimab every 6 weeks through a needle into a vein as an intravenous (IV) infusion for up to 2 years. People will take lenvatinib once a day as a capsule.

How is this study designed?

Both the people in the study and the researcher will know which study medicines a person is getting (**open-label study**).

People will have urine, blood, tumor, and imaging tests during the study. They will also:

- Have physical examinations
- Have pictures taken of their skin
- Answer questions about how they are feeling and their ability to carry out daily tasks

People may be in this study for about 2 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 study medicines are **safe** and how well people **tolerate** them	The number of people who: • Had an **adverse event (AE)** – an AE is a health problem that happens or worsens during a study • Stopped treatment due to an AE
To learn the **objective response rate (ORR)** of people who receive the study medicines	**ORR** is the number of people whose cancer **responds** to treatment (gets smaller or goes away) during the study
Other goal	**How it will be measured**
To learn more about the **cancer response** of people who receive the study medicines	During the study, researchers will measure: • **Duration of response (DOR)** - The length of time from when the cancer first responds to treatment until the cancer grows or spreads, or death from any cause • **Brain metastasis response rate** - The number of people whose brain tumors get smaller or go away • **Brain metastasis DOR -** The length of time from when the brain tumors get smaller or go away until the tumors grow or spread, or death from any cause • **Progression-free survival** - The length of time from the start of treatment until the cancer grows or spreads, or death from any cause

What are the possible benefits and risks?

People may or may not benefit from the treatment received during the study. More information about the benefits and risks is in the Investigator Brochure, Protocol, and Informed Consent documents.