Protocol Plain Language Summary

A clinical study of pembrolizumab with other medicines to treat skin cancer (MK-3475-02A)

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 02A

Why is this study needed?

Researchers are looking for new ways to treat people with melanoma that does not **respond** to treatment.

- **Melanoma** is a type of skin cancer that is more likely to grow and spread
- **Responding** means the cancer gets smaller or goes away

A standard treatment for melanoma may include **immunotherapy**. An immunotherapy is a treatment that helps the immune system fight cancer. **Pembrolizumab** is one type of immunotherapy that can be used to treat melanoma. Immunotherapy does not work to treat melanoma for some people.

Researchers want to know if adding other treatments to pembrolizumab can treat melanoma that did not respond.

The goals of this study are to learn:

- About the safety of pembrolizumab given with other treatments
- How well people tolerate the treatments
- How many people have melanoma that responds to the treatments

Who will take part in this study?

About 300 people with melanoma will be in this study. They will be 18 years or older and:

- Have melanoma that cannot be removed by surgery
- Have melanoma that did not respond to standard treatment
- Did not have another type of cancer in the past 2 years

What treatments are being given during the study?

People will receive 2 or 3 of these treatments:

- **Pembrolizumab** – an immunotherapy
- **Quavonlimab** – an immunotherapy
- **Vibostolimab** – an immunotherapy
- **Lenvatinib** – a targeted therapy. A targeted therapy works to control how specific types of cancer cells grow and spread.
- **All-trans retinoic acid (ATRA)** – a medicine that can slow or stop the growth of cancer cells

People will receive pembrolizumab, quavonlimab, and vibostolimab through a needle into a vein as an intravenous (IV) infusion every 3 or 6 weeks.

People will take lenvatinib by mouth every day. People will take ATRA by mouth for 3 days every 3 weeks.

People will receive their assigned treatments for up to about 2 years.

How is this study designed?

People will be assigned to one of these treatment groups:

- **Group A**: Pembrolizumab with quavonlimab and vibostolimab
- **Group B**: Pembrolizumab with quavonlimab and lenvatinib
- **Group C**: Pembrolizumab with ATRA

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

People may 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 about the **safety** of the treatments in Groups A, B, and C and how well people tolerate them	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 learn about the **objective response rate (ORR)** for Groups A, B, and C	**ORR** is the number of people whose cancer responds to treatment during the study
Other goal	**How it will be measured**
To learn about the **duration of response (DOR)** for Groups A, B, and C	**DOR** is the length of time from when the cancer first responds to 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.