Protocol Plain Language Summary

# A clinical study of pembrolizumab alone or with other treatments for skin cancer (MK-3475-02B)

**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 02B

## Why is this study needed?

Researchers are looking for new ways to treat advanced melanoma that has not been treated before. **Melanoma** is a type of skin cancer that is more likely to grow and spread. **Advanced** means the cancer has spread to other parts of the body (metastatic) and cannot be removed with surgery.

Standard treatment for melanoma may include **immunotherapy**, such as **pembrolizumab**. Immunotherapy is a treatment that helps the immune system fight cancer.

Researchers want to know if adding other treatments to pembrolizumab can treat advanced melanoma.

The goals of this study are to learn:

- About the safety and how well people tolerate pembrolizumab given with other treatments
- How many people have melanoma that responds (gets smaller or goes away) to treatment

## Who will take part in this study?

About 630 people with advanced melanoma will be in this study. They will be at least 18 years old and:

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

## What treatments are being given during the study?

People will receive **pembrolizumab**. They may also receive 1 or more of these treatments:

- **All-trans retinoic acid (ATRA)**, a medicine that makes it easier for your immune system to fight cancer
- **Favezelimab**, an immunotherapy
- **Lenvatinib**, a targeted therapy, which works on specific cancer cells to stop them from growing
- **Quavonlimab**, an immunotherapy
- **Vibostolimab**, an immunotherapy

People will receive immunotherapy treatments through a needle into a vein as an intravenous (IV) infusion every 3 or 6 weeks. People will take lenvatinib by mouth once every day. People will take ATRA by mouth twice a day for 3 days out of every 3 weeks.

## How is this study designed?

People will be assigned to one of these groups:

- **Group A**: Pembrolizumab and vibostolimab
- **Group B**: Pembrolizumab alone
- **Group C**: Pembrolizumab with quavonlimab
- **Group D**: Pembrolizumab with quavonlimab and lenvatinib
- **Group E**: Pembrolizumab with favezelimab
- **Group F**: Pembrolizumab with favezelimab and all-trans retinoic acid (ATRA)
- **Group G**: Pembrolizumab with favezelimab and vibostolimab

This study has 2 parts:

**Part 1:** The safety of the combination of ATRA or vibostolimab when given with pembrolizumab and favezelimab in Groups F and G will be tested in a small group of people. The dose of ATRA will be lowered if the first dose tested is not tolerated. Researchers will review the safety of the combination prior to giving the combination to all the people in Groups F and G during Part 2.

**Part 2:** People in every group will receive their assigned treatments for about 2 years until:

- The cancer grows or spreads
- They do not tolerate the treatment, or
- They stop the study

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 and pictures taken of their skin.

People may be in this study for about 2 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** and how well people **tolerate** the treatments | The number of people who:<br>• Have an **adverse event (AE).** An AE is a health problem that happens or worsens during a study<br>• Stop treatment due to an AE<br>• Have a dose-limiting toxicity (DLT) during the first 3 weeks of treatment in Part 1 only. A DLT is a medical problem related to the study medicine that prevents researchers from giving a higher dose |
| To learn about the **objective response rate (ORR)** for all groups | **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 all groups | **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.