Protocol Plain Language Summary

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

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 02C

Why is this study needed?

Researchers are looking for new ways to treat **melanoma** that has spread to **regional lymph nodes.** **Melanoma** is a type of skin cancer. **Lymph nodes** are small, bean-shaped organs that are part of the immune system. **Regional lymph nodes** are lymph nodes that are located near the melanoma.

Current treatment for melanoma that has spread to regional lymph nodes is surgery followed by immunotherapy. **Immunotherapy** is a treatment that helps the immune system fight cancer.

Researchers want to know if adding pembrolizumab alone or with other treatments before surgery, followed by pembrolizumab alone after surgery, can treat melanoma that has spread to regional lymph nodes.

The goals of this study are to learn:

- About the safety and how well people tolerate the treatments
- If treatment given before surgery can remove cancer cells in tumors and lymph nodes

Who will take part in this study?

About 140 people with melanoma that has spread to regional lymph nodes will be in this study. They will be at least 18 years old and:

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

What treatments are being given during the study?

Everyone will receive **pembrolizumab**. They may also receive one of these treatments:

- **Vibostolimab** – an immunotherapy
- **Gebasaxturev** – a virus that kills certain cancer cells
- **MK-4830** – an immunotherapy
- **Favezelimab** – an immunotherapy
- **All-trans retinoic acid (ATRA)** – a medicine that makes it easier for the immune system to fight cancer

People will receive pembrolizumab, vibostolimab, favezelimab, and MK-4830 through a needle into a vein as an intravenous (IV) infusion every 3 or 6 weeks. Gebasaxturev will be given as 5 shots, into the tumor, over 3 weeks. 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 and gebasaxturev
- **Group C**: Pembrolizumab alone
- **Group D**: Pembrolizumab and MK-4830
- **Group E**: Pembrolizumab and favezelimab
- **Group F**: Pembrolizumab and ATRA

People in all groups will receive their assigned treatment for 5 weeks. They will have surgery to remove the tumor and all regional lymph nodes. After surgery, researchers will check for cancer using imaging tests. People without signs of cancer will receive pembrolizumab alone for 11 months and be followed until the cancer comes back.

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

People may have urine, blood, tumor testing, and imaging tests during the study. They will also have physical examinations and photos taken of their skin.

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** and how well people **tolerate** the treatments	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 how many people in each group have a **pathological complete response (pCR)**	**pCR** means there are no signs of cancer cells in tumors and lymph nodes removed during surgery. Researchers will measure the number of people who have pCR.
Other goals	**How they will be measured**
To learn how many people in each group have a **near pCR**	**Near pCR** means there are 10% or fewer cancer cells remaining in tumors and lymph nodes removed during surgery. Researchers will measure the number of people who have near pCR.
To learn how many people in each group have a **partial pathological response (pPR)**	**pPR** means there are between 11% and 50% of cancer cells remaining in tumors and lymph nodes removed during surgery. Researchers will measure the number of people who have pPR.
To learn about the **recurrence-free survival (RFS)** for all groups	**RFS** is the length of time from surgery until the cancer comes back 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 Protocol.