Protocol Plain Language Summary

A clinical study of pembrolizumab for treating skin cancer after it has been removed by surgery (MK-3475-716)

Protocol Title: Adjuvant Therapy with Pembrolizumab versus Placebo in Resected High-risk Stage II Melanoma: A Randomized, Double-blind Phase 3 Study (KEYNOTE 716)

Why is this study needed?

Researchers are looking for new ways to treat people with melanoma**. Melanoma** is a type of skin cancer that can grow and spread. People with melanoma often have surgery to remove it. People who have a high chance (risk) of melanoma coming back after surgery may receive more treatment to reduce the chance of it coming back. Standard treatment after surgery is **immunotherapy**, which is a treatment that helps the immune system fight cancer. **Pembrolizumab** is an immunotherapy.

The goal of this study is to learn if people who receive pembrolizumab live longer without the cancer coming back or spreading than those who receive placebo. 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 954 people with melanoma will be in this study. They will be ages 12 years and older and:

- Had surgery to remove melanoma
- Have not been treated for melanoma except for surgery
- Do not have another cancer that was treated in the last 5 years

What treatments are being given during the study?

During this study, people may receive one or both of these:

- **Pembrolizumab,** the study medicine
- **Placebo**

People will receive treatment through a needle into a vein as an intravenous (IV) infusion once every 3 weeks.

How is this study designed?

People may be in this study for up to 15 years. This study has 2 Parts:

- **Part 1:** People will have an equal chance of receiving pembrolizumab or placebo for up to 1 year.
- **Part 2:** People from Part 1 who have melanoma come back may receive pembrolizumab for up to 2 years. This includes people who received either pembrolizumab or placebo in Part 1.

After treatment ends, researchers will contact people as long as they are alive, until they leave the study, or until the study ends.

Neither the people in the study nor the researchers will know which treatment a person receives in **Part 1** (double-blind). Both the people in the study and researchers will know which treatment the person receives in **Part 2** (open label).

During the study, people may give urine and blood samples, have tumor and imaging tests, have physical examinations, and answer questions about how they are feeling and their ability to carry out daily tasks.

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

Main goal	How it will be measured
To learn if people who receive pembrolizumab have longer **recurrence-free survival (RFS)** compared to people who receive placebo	**RFS** is the length of time from when people start the study until either the cancer comes back, cancer spreads, or death from any cause.
Other goals	**How they will be measured**
To learn if people who receive pembrolizumab have longer **distant metastasis-free survival (DMFS)** compared to people who receive placebo	**DMFS** is the length of time from the when people start the study until the cancer spreads from where it started to other parts of the body.
To learn if people who receive pembrolizumab have longer **overall survival (OS)** compared to people who receive placebo	**OS** is the length of time that people live from the start of the study until death from any cause.
To learn about the **safety** of pembrolizumab and how well people tolerate it	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

What are the possible benefits and risks?

People may or may not benefit from the treatment received during the study. The study has an external group of experts that oversees 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 Investigator Brochure, Protocol, and Informed Consent documents.