Protocol Plain Language Summary

Clinical study of pembrolizumab after surgery and radiation in people with advanced squamous cell skin cancer (MK-3475-630)

Protocol title: A Phase 3, Randomized, Double-blind, Placebo-controlled Study to Evaluate Pembrolizumab Versus Placebo as Adjuvant Therapy Following Surgery and Radiation in Participants with High-risk Locally Advanced Cutaneous Squamous Cell Carcinoma (LA cSCC) (KEYNOTE-630)

Why is this study needed?

Researchers are looking for new ways to prevent locally advanced cutaneous squamous cell carcinoma (LA cSCC) from coming back after treatment. **LA cSCC** is skin cancer that has spread deeper into tissues, muscles, or nerves below the skin, but has not spread to other body parts. Surgery to remove the cancer and radiation therapy works well to treat most people with LA cSCC. But some people have a high chance of LA cSCC coming back and spreading, which can be deadly.

Pembrolizumab is an immunotherapy, which is a treatment that helps the immune system fight cancer. **Adjuvant treatment** is given after the first (main) treatment to prevent cancer from coming back.

The goal of this study is to learn if taking pembrolizumab as adjuvant treatment can help people live longer without the cancer coming back.

Who will take part in this study?

About 430 people with LA cSCC will be in this study. They will be ages 18 and older and have:

- Had surgery and radiation that worked to treat the LA cSCC
- Increased chance of the LA cSCC coming back
- Had high risk LA cSCC that forms, grows, or spreads quickly
- No signs of cancer when they join the study

How is this study designed?

People may be in this study for up to 8 years. This study has 3 Parts:

- **Part 1** (about 1 year)**:** People will have an equal chance of receiving pembrolizumab or a placebo once every 6 weeks for up to 9 cycles (1 cycle is 6 weeks). In this part, neither the people in the study nor the researchers will know which treatment a person receives (double-blind).
- **Part 2** (until 5 years after they joined the study)**:** People who had the cancer come back and cannot have surgery to remove it may receive pembrolizumab once every 6 weeks for up to 18 cycles (about 2 years). This may include:
  - People assigned the placebo in Part 1 who cross-over to receive pembrolizumab in Part 2
  - People who received pembrolizumab in Part 1 and had LA cSCC come back more than 6 months after completing 1 year of pembrolizumab

  In this part, both the people in the study and researchers will know which treatment the person receives because everyone receives pembrolizumab (open-label).
- **Follow-up** (until the study ends)**:** After each person's treatment ends, researchers will contact people every 12 weeks as long as they are alive, until they leave this study, or until the study ends.

During the study, people may have tumor, blood, urine, and imaging tests, have physical examinations, and answer sets of questions about their health.

What treatments are being given during the study?

Treatments are received through a vein, which is called an intravenous (IV) infusion. During this study, people may receive one or both of these:

- **Pembrolizumab**
- **Placebo:** A placebo is a look-alike substance that does not contain any medicine. Using a placebo helps researchers better understand the real effects of the study medicine.

People assigned to receive the placebo may switch to pembrolizumab.

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

Main goal (Primary Objective)	How it will be measured
To learn if people who receive pembrolizumab live longer without the cancer coming back compared to those who receive placebo	**Recurrence free survival:** the length of time from when the person starts the study until any of the following: • The LA cSCC comes back as the recurrence or high risk new primary cSCC, • The LA cSCC spreads, or • Death due to any cause
Other goals (Secondary Objectives)	**How they will be measured**
To learn if people who receive pembrolizumab live longer compared to those who receive placebo	**Overall survival:** the average length of time that people live from the start of treatment until death from any cause
To learn about the **health-related quality of life (HRQoL)** of people who receive pembrolizumab compared to those who receive placebo	People will answer sets of questions to measure their HRQoL, including questions about their overall health and ability to complete physical tasks, such as swallowing and talking
To learn about the safety and how well people tolerate pembrolizumab	During the study, 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

What are the possible benefits and risks?

People in this study may not get a direct benefit of treatment, such as the cancer stops growing or goes away. This study has a Data Monitoring Committee that oversees the study's overall risk and benefit. If this committee decides that the study treatment is not safe or is unlikely to stop the cancer growing or spreading, the study can be stopped.

More information about benefits and risks may be found in the Investigator's Brochure, Protocol, and Informed Consent documents.