Protocol Plain Language Summary

A clinical study of pembrolizumab in people with endometrial cancer (MK-3475-B21)

Protocol Title: A Phase 3, Randomized, Double-Blind Study of Pembrolizumab versus Placebo in Combination With Adjuvant Chemotherapy With or Without Radiotherapy for the Treatment of Newly Diagnosed High-Risk Endometrial Cancer After Surgery With Curative Intent (KEYNOTE-B21 / ENGOT-en11 / GOG-3053).

Why is this study needed?

Researchers are looking for new ways to treat people with **high-risk endometrial cancer (EC)** who have had surgery to remove the cancer. EC is cancer that starts in the tissues inside the uterus (womb). **High-risk** means cancer has a high chance of coming back after surgery.

The first treatment for EC is usually surgery to remove the cancer and the uterus, ovaries, and fallopian tubes. After surgery, the **standard treatment** (usual treatment) includes **chemotherapy** with or without **radiation therapy**. Chemotherapy is medicine that destroys cancer cells or stops them from growing. Radiation therapy is a treatment that uses beams of intense energy (like X-rays) to shrink or get rid of tumors.

Pembrolizumab, the study medicine, is an immunotherapy, which is a treatment that helps the immune system fight cancer.

The goal of this study is to learn if people who receive pembrolizumab and standard treatment live longer without EC coming back and live longer overall compared to people who receive a **placebo** and standard treatment. A **placebo** looks like the study medicine but has no study medicine in it. Using a placebo helps researchers better understand if the study medicine works.

Who will take part in this study?

About 990 females with high-risk EC will be in the study. They will be 18 years old and older and:

- Had surgery to remove the cancer and have no signs of cancer after surgery
- Have not received previous cancer treatment, except for surgery

What treatments are being given during the study?

People will have an equal chance of receiving either:

- **Pembrolizumab and standard treatment**
- **Placebo and standard treatment**

Standard treatment is chemotherapy with or without radiation therapy. The study doctor will decide if a person will receive radiation therapy. Chemotherapy, pembrolizumab, and placebo are given through a needle into a vein as an intravenous (IV) infusion.

How is this study designed?

There are 2 treatment stages for each person in this study:

- **Stage 1**: People will receive pembrolizumab or placebo every 3 weeks for about 4 months. They will receive chemotherapy every 3 weeks for up to 4 months.
- **Stage 2**: People will receive pembrolizumab or placebo every 6 weeks for about 8 and a half months. They will not receive chemotherapy.

If the study doctor decides a person will receive radiation therapy, they will receive it in both stages.

Neither the people in the study nor the researchers will know if a person is receiving pembrolizumab or placebo (**double-blind study**). During the study, people may give urine and blood samples, have tumor and imaging tests, physical examinations, and answer questions about how they are feeling and their ability to carry out daily tasks.

A person may be in this study for up to 4 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 if people who receive pembrolizumab and standard treatment have longer **disease-free survival (DFS)** compared to people who receive placebo and standard treatment	**DFS** is the length of time people are alive without the cancer coming back after the start of treatment
To learn if people who receive pembrolizumab and standard treatment have longer **overall survival (OS)** compared to people who receive placebo and standard treatment	**OS** is the length of time that people are alive from the start of treatment until death from any cause

Other goals	How they will be measured
To learn **more about DFS** of people who receive pembrolizumab and standard treatment compared to people who receive placebo and standard treatment	During the study, experts who are not involved with the study will measure **DFS** for all people in the study
To compare **DFS and OS in people with different types of tumors** who receive pembrolizumab and standard treatment to people who receive placebo and standard treatment	Researchers will measure **DFS** and **OS** in: • People whose cancer has **PD-L1** – PD-L1 is a type of protein found on cancer cells that can help the cancer hide from the body's immune system • Groups of people with different **gene mutations** (changes in the order of DNA in cancer cells)
To learn if pembrolizumab and standard treatments are **safe** and how well people **tolerate** them	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
To compare the **quality of life (QoL)** of people who receive pembrolizumab and standard treatment to people who receive placebo and standard treatment	People will answer sets of questions to measure their **QoL**, including questions about their overall health and their ability to carry out daily tasks. Researchers will measure the change in scores during the study.

What are the possible benefits and risks?

People may or may not benefit from the treatment received during the study. This study has an external group of experts that will oversee 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.