Protocol Plain Language Summary

A clinical study of pembrolizumab and chemotherapy to treat breast cancer (MK-3475-B49)

Protocol Title: A Randomized, Double-blind, Placebo-controlled, Phase 3 Study of Pembrolizumab Plus Chemotherapy Versus Placebo Plus Chemotherapy for the Treatment of Chemotherapy-Candidate Hormone Receptor-Positive, Human Epidermal Growth Factor Receptor 2-Negative (HR+/HER2-) Locally Recurrent Inoperable or Metastatic Breast Cancer (KEYNOTE-B49)

Why is this study needed?

Researchers are looking for other ways to treat people with **metastatic breast cancer (MBC)** that is **hormone receptor-positive** and **human epidermal growth factor receptor 2-negative (HR+/HER2-)**:

- **Metastatic** means the cancer has spread to other parts of the body and cannot be removed by surgery
- **HR positive** means the cancer cells have proteins that attach to estrogen or progesterone (hormones) which help the cancer to grow and spread
- **HER2 negative** means the cancer cells have a low amount of a protein called HER2

Chemotherapy and immunotherapy are treatments for people with MBC. **Chemotherapy** is medicine that destroys cancer cells or stops them from growing**. Immunotherapy** is a treatment that helps the immune system fight cancer. **Pembrolizumab**, the study medicine, is an immunotherapy.

The goal of this study is to learn if people who receive pembrolizumab and chemotherapy live longer overall and without the cancer getting worse compared to people who receive placebo and chemotherapy. 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 800 people with HR+/HER2- MBC will be in this study. They will be at least 18 years old and:

- Have not received chemotherapy to treat MBC
- Have tumors that are positive for 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.
- Not have certain heart disease

What treatments are being given during the study?

People will have an equal chance to receive one of these treatments:

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

People will receive pembrolizumab or placebo once every 3 weeks through a needle into a vein as an intravenous (IV) infusion. Chemotherapy may be given either as tablets or through an IV infusion. The type and schedule of chemotherapy will be based on the researcher's choice.

People will continue their treatment until the cancer gets worse or the person doesn't tolerate it.

How is this study designed?

Neither the people in the study nor the researchers will know which treatment a person is taking (double-blind study). During the study, people may give urine and blood samples, have imaging tests and 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 about 6 years.

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

Main goals	How they will be measured
To learn if the **progression-free survival (PFS)** of people who receive pembrolizumab and chemotherapy is longer than those who receive placebo and chemotherapy	**PFS** is the length of time from when the person starts the study until the cancer grows or spreads, or death from any cause. This will be measured by experts that are not linked to the study.
To learn if the **overall survival (OS)** of people who receive pembrolizumab and chemotherapy is longer than those who receive placebo and chemotherapy	**OS** is the length of time from when the person starts the study until death from any cause.

Other goals	How they will be measured
To compare the **PFS** of people who receive pembrolizumab and chemotherapy to those who receive placebo and chemotherapy	During the study, researchers will measure the **PFS**.
To compare the **cancer response** in people who receive pembrolizumab and chemotherapy to those who receive placebo and chemotherapy	During the study, researchers will measure: • **Objective response rate (ORR)**: the number of people whose cancer responds to treatment (gets smaller or goes away) • **Disease control rate (DCR)**: the number of people who have the cancer stop growing or get smaller, or show no signs of cancer for at least 6 months • **Duration of response (DOR)**: the length of time from when the cancer first responds to treatment until the cancer grows, spreads, or death from any cause
To learn about people's **health-related quality of life (HRQoL)**	People will answer sets of questions to measure their **HRQoL**, including questions about their overall health and their ability to carry out daily tasks. Researchers will measure: • The change in the scores during the study • The length of time from when the person starts the study until their HRQoL gets worse
To learn about the **safety** and how well people **tolerate** pembrolizumab and chemotherapy	During the study, the number of people who: • Have an **adverse event (AE)** – An AE is a health problem that happens or worsens • Stop 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. This study has an external group of experts who 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 protocol.