Protocol Plain Language Summary

A clinical study of pembrolizumab alone or combined with other immunotherapies to treat people with colorectal cancer (MK-1308A-008)

Protocol Title: A Phase 2, Multicenter, Multi Arm, Study to Evaluate MK-1308A (Co-formulated quavonlimab (MK-1308)/pembrolizumab) Versus Other Treatments in Participants with Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Stage IV Colorectal Cancer: (MK-1308A-008)

Why is this study needed?

Researchers are looking for other ways to treat people with **metastatic colorectal cancer (mCRC)** that have **mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H)** tumors:

- **Colorectal cancer** is cancer that starts in the colon or rectum, which is the last part of the digestive system where stool is stored until it's passed
- **Metastatic** means the cancer has spread to other parts of the body
- **dMMR** means that cells can't fix changes (mutations) that happen in the cell, which can lead to cancer
- **MSI-H** means there are many changes in the cancer cells DNA

Chemotherapy and immunotherapy are treatments for mCRC**. Chemotherapy** is medicine that destroys cancer cells or stops them from growing. **Immunotherapy** is a treatment that helps the immune system fight cancer. **Pembrolizumab combined with other immunotherapies** are the study medicines. The goal of this study is to compare pembrolizumab alone to pembrolizumab combined with other immunotherapies.

Researchers want to learn how many people respond (cancer gets smaller or goes away) to pembrolizumab alone or combined with other immunotherapies.

Who will take part in this study?

About 320 people with mCRC that is dMMR and MSI-H will be in this study. They will be at least 18 years old and:

- Have either:
  - Had certain chemotherapy treatments for mCRC but stopped responding or could not tolerate it, or
  - Have not had certain treatment for mCRC in the past
- Not have certain health conditions
- Have not had the cancer spread to their brain or spine

What treatments are being given during the study?

Not all treatments will be given to all countries. People will receive one of these immunotherapy treatments through a needle into a vein as an intravenous (IV) infusion every 3 or 6 weeks for up to about 2 years:

- **Pembrolizumab with quavonlimab**
- **Pembrolizumab with vibostolimab**
- **Favezelimab with pembrolizumab**
- **MK-4830 and pembrolizumab**
- **Pembrolizumab alone**

How is this study designed?

People will be assigned to a group based on if they've had previous treatment for mCRC or not:

- **Group A**: People who had certain chemotherapy treatments will have an equal chance to receive 1 of 2 treatments:
  - Pembrolizumab with quavonlimab
  - Pembrolizumab alone
- **Group B**: People who have not had previous treatment for mCRC will have an equal chance to receive 1 of 5 treatments:
  - Pembrolizumab with quavonlimab
  - Pembrolizumab with vibostolimab
  - Favezelimab with pembrolizumab
  - MK-4830 and pembrolizumab
  - Pembrolizumab alone

Not all groups will be open in all countries. Both the people in the study and the researcher will know which study treatment a person is getting (open-label study). During the study, people may give urine and blood samples, have imaging tests and physical examinations, have a test to measure the heart's electrical activity (called an electrocardiogram or ECG), 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 about 3 years.

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

Main goal	How it will be measured
To compare the **objective response rate (ORR)** in people who receive pembrolizumab alone or combined with other immunotherapies	**ORR** is the number of people whose cancer responds to treatment (gets smaller or goes away). This will be measured by experts that are not linked to the study site and do not know which treatment people received.

Other goals	How they will be measured
To learn about the **duration of response (DOR)** in people who receive pembrolizumab alone or combined with other immunotherapies	**DOR** is the length of time from when the cancer first responds to treatment until the cancer grows, spreads, or death from any cause.
To compare **how long the cancer responds** in people who receive pembrolizumab alone or combined with other immunotherapies	Researchers will measure responses throughout the study: • **Progression-free survival (PFS)**: the length of time from the start of treatment until the cancer grows or spreads, or death from any cause. • **Overall survival (OS)**: the length of time that people live from the start of treatment until death from any cause

To compare the **ORR** in people who receive pembrolizumab alone or combined with other immunotherapies	Study researchers will measure ORR during the study.
To learn about the **safety** and how well people **tolerate** pembrolizumab alone or combined with other immunotherapies	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.

More information about the benefits and risks is in the Investigator Brochure, Protocol, and Informed Consent documents.