Protocol Plain Language Summary

A clinical study of pembrolizumab and chemotherapy to treat advanced biliary tract cancer (MK-3475-966)

Protocol Title: A Phase 3 Randomized, Double Blind Study of Pembrolizumab Plus Gemcitabine/Cisplatin versus Placebo Plus Gemcitabine/Cisplatin as First-Line Therapy in Participants with Advanced and/or Unresectable Biliary Tract Carcinoma

Why is this study needed?

Researchers are looking for new ways to treat people with **advanced biliary tract cancer (BTC)**. BTC is cancer in the gallbladder or tubes (ducts) that carry a digestive fluid called bile. Advanced means the cancer has spread to other parts of the body or cannot be removed with surgery.

The standard treatment for people with advanced BTC is chemotherapy. **Chemotherapy** is medicine that destroys cancer cells or stops them from growing. **Pembrolizumab**, the study medicine, is an immunotherapy. **Immunotherapy** is a treatment that helps the immune system fight cancer. Researchers want to learn if giving pembrolizumab and chemotherapy can treat advanced BTC.

The goal of this study is to learn if people who receive pembrolizumab and chemotherapy live longer overall 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 a study medicine.

Who will take part in this study?

About 1,048 people with advanced BTC will be in this study. They will be at least 18 years old and:

- Have not received certain treatments for BTC in the past
- Have not had other certain types of cancer in the past 3 years

What treatments are being given during the study?

People will have an equal chance to receive one of these treatments through a needle into a vein as an intravenous (IV) infusion:

- **Pembrolizumab** (the study medicine) and **chemotherapy**
- **Placebo** and **chemotherapy**

People will receive pembrolizumab or placebo once every 3 weeks for up to about 2 years unless the cancer gets worse, or the person doesn't tolerate treatment.

People will receive 2 types of chemotherapy once a week for 2 out of every 3 weeks:

- one type of chemotherapy for up to about 6 months
- the other type of chemotherapy 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 will give urine, blood, and tumor tissue 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 3 years.

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

Main goal	How it will be measured
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 that people live from the start of the study until death from any cause.
Other goals	**How they will be measured**
To learn about the **cancer response** in people who receive pembrolizumab and chemotherapy compared to those who receive placebo and chemotherapy	During the study, researchers will measure: • **Progression-free survival (PFS)**: the length of time from the start of the study until the cancer grows or spreads, or death from any cause • **Objective response rate (ORR)**: the number of people whose cancer responds to treatment (gets smaller or goes away)
To learn about the **duration of response (DOR)** in people who receive pembrolizumab or placebo and chemotherapy	**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 learn about the **safety** of pembrolizumab and chemotherapy and how well people **tolerate** them	During the study, the number of people who: • Had an **adverse event (AE)**—An AE is health problem that happens or worsens • 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. 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.