Protocol Plain Language Summary

A clinical study of lenvatinib, pembrolizumab, and chemotherapy for treating esophageal cancer (MK-7902-014)

Protocol Title: A Phase 3, Randomized Study to Evaluate the Efficacy and Safety of Pembrolizumab (MK-3475) + Lenvatinib (E7080/MK-7902) + Chemotherapy Compared with Standard of Care as First-line Intervention in Participants with Metastatic Esophageal Carcinoma

Why is this study needed?

Researchers are looking for new ways to treat people with metastatic **esophageal cancer**. Esophageal cancer starts in the lining of the **esophagus.** The esophagus is the tube that connects the throat to the stomach. **Metastatic** means cancer has spread to other parts of the body.

Standard treatment for esophageal cancer is chemotherapy and an **immunotherapy**, such as **pembrolizumab**. **Chemotherapy** is a medicine that works to destroy cancer cells or stop them from growing. An **immunotherapy,** including **pembrolizumab,** is a treatment that helps the immune system fight cancer.

Researchers want to learn if adding lenvatinib to standard treatment can help treat esophageal cancer. **Lenvatinib** (the study medicine) is a **targeted therapy**. A targeted therapy works to control how specific types of cancer cells grow and spread.

The goals of this study are to learn:

- about the safety of lenvatinib and standard treatment and how well people tolerate the treatments
- if people who receive lenvatinib and standard treatment live longer compared to standard treatment alone
- if people who receive lenvatinib and standard treatment live longer without the cancer growing or spreading compared to standard treatment alone

Who will take part in this study?

About 862 people with metastatic esophageal cancer will be in this study. They will be ages 18 years and older and:

- Have not been previously treated for metastatic esophageal cancer
- Do not have cancer that has spread to the brain or the spine

What treatments are being given during the study?

During this study, people will receive one of these treatments:

- **Lenvatinib** (study medicine) **and standard treatment** (pembrolizumab and chemotherapy)
- **Standard treatment alone**

People will take lenvatinib once a day by mouth until the cancer grows or spreads, or the person cannot tolerate the treatment.

People will receive pembrolizumab through a vein by intravenous (IV) infusion every 6 weeks for up to 2 years. People will receive chemotherapy by IV infusion every 2 or 3 weeks depending on the type of chemotherapy. Chemotherapy will be given for up to 2 years.

How is this study designed?

People may be in this study for up to 5 years. This study has 2 parts:

- **Part 1:** About 12 people will receive lenvatinib and standard treatment. People will have an equal chance of receiving 1 of 2 different types of chemotherapy. Researchers want to see if the treatments are safe in a small group of people before giving them to a larger group in Part 2.
- **Part 2:** About 850 people will have an equal chance of receiving either:
  - Lenvatinib and standard treatment
  - Standard treatment alone

  The researcher will choose the type of chemotherapy people will receive in Part 2.

Both the people in the study and researchers will know which treatment the person receives (open label study).

During the study, people may give urine and blood samples, have tumor and imaging tests, have physical examinations, and answer questions about how they are feeling and their ability to carry out daily tasks.

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

Main goals	How they will be measured
To learn about the **safety** of lenvatinib and standard treatment and how well people **tolerate** the treatments in Part 1	Number of people in Part 1 who: • Have a **dose limiting toxicity (DLT)** during the first 3 weeks of treatment. A DLT is a medical problem related to the study medicine that prevents giving a higher dose • Have an **adverse event (AE)**. An AE is a health problem that happens or worsens during the study • Stop treatment due to an AE
To learn about the **cancer response** of people who receive lenvatinib and standard treatment compared to those who receive standard treatment alone in Part 2	Researchers will measure these cancer responses during Part 2: • **Overall survival (OS)**: the length of time that people live from the start of the study until death from any cause • **Progression free survival (PFS)**: the length of time from the start of the study until the cancer gets worse or death from any cause
Other goals	**How they will be measured**
To learn about the **cancer response** of people who receive lenvatinib and standard treatment compared to those who receive standard treatment alone in Part 2	Researchers will measure these responses during Part 2: • **Objective response rate (ORR)**: the number of people whose cancer responds to treatment (cancer gets smaller or goes away) • **Duration of response (DOR)**: the length of time from when the cancer first responds to treatment until the cancer gets worse or death from any cause These responses will be measured in people whose tumors have a certain protein found on the cancer cells**:** • **OS** • **PFS** • **ORR** • **DOR**
To learn about the **safety** of lenvatinib and standard treatment and how well people **tolerate** the treatments in Part 2	Number of people in Part 2 who: • Have an AE during the study • Stop treatment due to an AE

To learn about the **quality of life (QoL)** of people who receive lenvatinib and standard treatment in Part 2	During the study, people will answer questions to measure **QoL**. The questions are about how they are feeling, esophageal cancer symptoms, and their ability to carry out daily tasks**.** Researchers will measure: • The change in the scores during the study • The length of time from the start of the study until QoL gets worse

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.