Protocol Plain Language Summary

# A clinical study of lenvatinib, pembrolizumab, and chemotherapy for treating stomach and esophageal cancer (MK-7902-015)

**Protocol Title:** A Phase 3, Randomized Study to Evaluate the Efficacy and Safety of Lenvatinib (E7080/MK-7902) plus Pembrolizumab (MK-3475) plus Chemotherapy Compared with Standard of Care Therapy as First-line Intervention in Participants with Advanced/Metastatic Gastroesophageal Adenocarcinoma (LEAP-015)

## Why is this study needed?

Researchers are looking for new ways to treat people with metastatic stomach cancer and a certain type of **esophageal** cancer**.** 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 stomach and esophageal cancer is **chemotherapy**. **Chemotherapy** is a medicine that works to destroy cancer cells or stop them from growing. These cancers may also be treated with a combination of chemotherapy and **immunotherapy**, such as **pembrolizumab**. An **immunotherapy** is a treatment that helps the immune system fight cancer.

Researchers want to learn if adding **lenvatinib** to chemotherapy and pembrolizumab can help treat stomach and 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, pembrolizumab, and chemotherapy and how well people tolerate the treatments
- if people who receive lenvatinib with pembrolizumab and chemotherapy live longer overall and without the cancer growing or spreading compared to chemotherapy alone

## Who will take part in this study?

About 890 people with metastatic stomach or a certain type of esophageal cancer will be in this study. They will be 18 years or older and:

- Have not been previously treated for stomach or esophageal cancer
- Have not been previously treated with immunotherapy

## What treatments are being given during the study?

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

- Lenvatinib (the study medicine)
- Pembrolizumab
- Chemotherapy

People will take lenvatinib once a day by mouth. People will continue lenvatinib until the cancer gets worse or the person does not tolerate it. Pembrolizumab will be given through a vein by intravenous (IV) infusion every 6 weeks for up to 2 years. People will receive chemotherapy according to the suggested schedule for the type of chemotherapy used. After people finish chemotherapy, they will increase the amount of Lenvatinib they take.

## How is this study designed?

This study has 2 parts:

- **Part 1:** About 12 people will receive lenvatinib with pembrolizumab and chemotherapy. Researchers will check if the treatments are safe in a small group of people before giving them to a larger group in Part 2.
- **Part 2:** About 878 people will have an equal chance of receiving either:
  - Lenvatinib with pembrolizumab and chemotherapy
  - Chemotherapy alone

People will receive lenvatinib with pembrolizumab and chemotherapy in both Parts 1 and 2. They will receive the treatment for about 3 months as **induction** therapy, followed by **consolidation** therapy. **Induction** therapy is the first therapy used to treat cancer. Chemotherapy is stopped after induction therapy. People will continue to receive lenvatinib with pembrolizumab as **consolidation** therapy. **Consolidation** therapy is used after the first therapy to destroy remaining cancer cells.

The researcher will choose the type of chemotherapy people will receive.

Both the people in the study and the researcher will know which study medicines a person is getting (called an open-label study).

People may have urine, blood, heart, tumor, and imaging tests during the study. They will also have physical examinations and answer questions about how they are feeling and their ability to carry out daily tasks.

People may be in this study for up to 4 years.

## 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, pembrolizumab, and chemotherapy and how well people **tolerate** the treatments in Part 1 | The number of people who:<br>• 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<br>• Have an **adverse event (AE)**. An AE is a health problem that happens or worsens during the study<br>• Stop treatment due to an AE |
| To learn about the **cancer response** of people who receive lenvatinib with pembrolizumab and chemotherapy compared to those who receive chemotherapy alone in Part 2 | Researchers will measure these cancer responses:<br>• **Overall survival (OS)**: the length of time that people live from the start of the study until death from any cause<br>• **Progression free survival (PFS)**: the length of time from the start of the study until the cancer gets worse or death from any cause<br><br>Responses will be measured in everyone in the study and in people with tumors that have different amounts of a certain protein found on the cancer cells called PD-L1. **PD-L1** can help the cancer hide from the immune system. |
| **Other goals** | **How they will be measured** |

| | |
|---|---|
| To learn more about the **cancer response** of people who receive lenvatinib with pembrolizumab and chemotherapy compared to those who receive chemotherapy alone in Part 2 | Researchers will measure these responses during the study:<br>• **Objective response rate (ORR)**: the number of people whose cancer responds to treatment (cancer gets smaller or goes away)<br>• **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<br><br>Responses will be measured in everyone in the study and in people with tumors that have different amounts of PD-L1. |
| To learn about the **safety** of lenvatinib, pembrolizumab, and chemotherapy and how well people **tolerate** the treatments in Part 2 | The number of people who:<br>• Have an AE during the study<br>• 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 that oversees 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.