Protocol Plain Language Summary

A clinical study of pembrolizumab with chemotherapy and radiation therapy in people with esophageal cancer (MK-3475-975)

Protocol title: A Randomized, Double-blind, Placebo-controlled Phase 3 Trial of Pembrolizumab (MK-3475) Versus Placebo in Participants with Esophageal Carcinoma Receiving Concurrent Definitive Chemoradiotherapy (KEYNOTE 975)

Why is this study needed?

Researchers are looking for new ways to treat esophageal cancer that has spread to lymph nodes. **Esophageal cancer** is a cancer that starts in the lining of the esophagus, which is the tube that connects the throat to the stomach. **Lymph nodes** are small bean-shaped organs that are part of the body's immune system.

Esophageal cancer is often first treated with surgery to remove the cancer. Not all people can have surgery due to the size or location of the cancer or because they choose not to have surgery. The current standard of care (**standard treatment)** for people who do not have surgery is both:

- **Chemotherapy** – a treatment that uses medicine to shrink or get rid of cancer
- **Radiation therapy** – a treatment that uses beams of intense energy (like X-rays) to shrink or get rid of cancer

Researchers want to know if adding pembrolizumab to the standard treatment can help treat esophageal cancer in people who cannot have surgery. **Pembrolizumab** is an immunotherapy, which is a treatment that helps the immune system fight cancer.

Researchers want to see if people who receive pembrolizumab with standard treatment live longer without their cancer growing or spreading and live longer overall.

Who will take part in this study?

About 700 people with esophageal cancer will be in this study. They will be aged 18 years and older and:

- Not able to have surgery to remove their tumor
- Not have metastatic esophageal cancer, which means the cancer has not spread from the esophagus to other parts of the body
- Have not had previous treatment for esophageal cancer

What treatments are being given during the study?

During this study, all people will receive the **standard treatment** of chemotherapy and radiation therapy. Along with the standard treatment, people will be assigned by equal chance to receive one of these:

- **Pembrolizumab** (the study medicine) given once every 3 or 6 weeks through a vein (intravenous, or IV, infusion) for up to 1 year
- **Placebo** given once every 3 or 6 weeks by IV infusion for up to 1 year. 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.

For the standard treatment, everyone will receive:

- Chemotherapy given by IV infusion for up to 11 weeks
- Radiation therapy for up to 6 weeks

How is this study designed?

Neither the people in the study nor the researchers will know which treatment a person receives (**double-blind**).

During the study, people may:

- Have blood, tumor, urine, and imaging tests
- Have physical examinations
- Answer sets of questions

People may be in this study for up to 6 years.

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

Main goals	How they will be measured
To compare **event free survival** for people receiving pembrolizumab and standard treatment to people receiving placebo and standard treatment	The length of time people are alive during the study without the cancer growing, spreading, or coming back
To compare **overall survival** for people receiving pembrolizumab and standard treatment to people receiving placebo and standard treatment	The length of time that people are alive after joining the study
Other goal	**How it will be measured**
To learn about the **safety** and how well people **tolerate** pembrolizumab and standard treatment	The number of people who: • Had an **adverse event (AE)** during the study – an AE is a health problem that happens or worsens during the study • Stopped treatment due to an AE

What are the possible benefits and risks?

People in this study may or may not have their cancer stop growing or go away. 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.