

Protocol Plain Language Summary

A clinical study of pembrolizumab with trastuzumab and chemotherapy for treating stomach (gastric) or gastroesophageal junction cancer (MK-3475-811)

Protocol Title: A Phase III, Randomized, Double-blind Trial Comparing Trastuzumab Plus Chemotherapy and Pembrolizumab With Trastuzumab Plus Chemotherapy and Placebo as First-line Treatment in Participants With HER2 Positive Advanced Gastric or Gastroesophageal Junction Adenocarcinoma (KEYNOTE 811)

Why is this study needed?

Researchers are looking for new ways to treat people with locally advanced, unresectable, or **metastatic stomach or gastroesophageal junction (GEJ) cancer** that is **HER2 positive**. The **GEJ** is where the esophagus (tube that carries food from the throat to the stomach) meets the stomach. Locally advanced means the cancer has spread to nearby tissues and muscles but has not spread to other parts of the body. Unresectable means the cancer cannot be removed with surgery. **Metastatic** means cancer has spread to other parts of the body. **HER2 positive** means the cancer cells make too much of the protein called HER2, which causes cancer to grow and spread quickly.

Standard treatment for stomach and GEJ cancer with HER2 is **chemotherapy** and **trastuzumab**. **Chemotherapy** is a medicine that works to destroy cancer cells or stop them from growing. Trastuzumab is an **immunotherapy**, which is a treatment that helps the immune system fight cancer.

Researchers want to know if adding **pembrolizumab**, another immunotherapy, to standard treatment can treat stomach and GEJ cancer that is HER2 positive.

The goal of this study is to learn if people who receive pembrolizumab and standard treatment live longer overall and without the cancer growing or spreading than people who receive placebo and standard treatment. 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 732 people with locally advanced, unresectable, or metastatic stomach or GEJ cancer will be in this study. They will be 18 years or older and:

- Have cancer that is HER2 positive
- Have not been previously treated for stomach or GEJ cancer

What treatments are being given during the study?

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

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

People will receive pembrolizumab or placebo through a vein by intravenous (IV) infusion every 3 weeks. They will receive treatment for up to 2 years or until the cancer gets worse or they do not tolerate it.

People will receive trastuzumab by IV infusion. People will receive the researcher's choice of chemotherapy by IV infusion or by mouth, based on the type of chemotherapy. People may receive trastuzumab and chemotherapy for up to 3 years (1 more year after pembrolizumab or placebo stops) or until the cancer gets worse or they do not tolerate treatment.

How is this study designed?

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

People may have urine, blood, 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 5 years.

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

Main goal	How it will be measured
To learn about the cancer response of people who receive pembrolizumab with trastuzumab and chemotherapy compared to those who receive placebo with trastuzumab and chemotherapy	Researchers will measure these cancer responses: <ul style="list-style-type: none"> • 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 more about the cancer response of people who receive pembrolizumab with trastuzumab and chemotherapy compared to those who receive placebo with trastuzumab and chemotherapy	Researchers will measure these responses during the study: <ul style="list-style-type: none"> • 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
To learn about the safety of pembrolizumab with trastuzumab and chemotherapy and how well people tolerate the treatments	The number of people who: <ul style="list-style-type: none"> • Have an AE during the study. An AE is a health problem that happens or worsens during a study • 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 who 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.