Protocol Plain Language Summary

Study of pembrolizumab in people with locally advanced head and neck region cancer (MK-3475-689)

Protocol title: A Phase III, Randomized, Open-label Study to Evaluate Pembrolizumab as Neoadjuvant Therapy and in Combination With Standard of Care as Adjuvant Therapy for Stage III-IVA Resectable Locoregionally Advanced Head and Neck Squamous Cell Carcinoma (LA HNSCC)

Why is this study needed?

Researchers are looking for new ways to treat locally advanced head and neck squamous cell carcinoma (LA HNSCC). **LA HNSCC** is a type of cancer that starts in the head and neck and spreads to other areas next to the original location. To treat LA HNSCC, people get surgery to remove the cancerous tumor. After surgery, people may receive additional standard of care therapy, radiation therapy with or without chemotherapy, known as **adjuvant therapy**.

Pembrolizumab is an immunotherapy, which is a treatment that helps the immune system fight cancer. In this study, researchers want to learn if people who receive pembrolizumab before surgery (**neoadjuvant treatment**) and after surgery live longer without the cancer growing, spreading, or coming back than people who receive standard of care.

Who will take part in this study?

About 704 people with LA HNSCC will be in this study. They will be ages 18 and older and:

- Have stage 3 or 4A LA HNSCC that can be removed with surgery
- Have HNSCC in the mouth, throat, or voice box

How is this study designed?

People may be in this study for up to 5 years. The person and researchers will know what treatment the person is receiving in this study (an open-label study). This study is separated into 2 parts occurring before and after surgery.

Part 1 (before surgery): People will have an equal chance of receiving either:

- **Pembrolizumab** once every 3 weeks for 6 weeks (2 cycles)
- **No treatment** before surgery

Part 2 (after surgery): Researchers will look at the tumor removed during surgery and put people into groups based on the chance (risk) of cancer coming back. The table below shows the groups:

	Part 2 Treatment	
	High risk group	**Low risk group**
Pembrolizumab prior to surgery	• Pembrolizumab every 3 weeks for 45 weeks (15 cycles) • Radiation • Chemo every 3 weeks for 9 weeks (3 cycles)	• Pembrolizumab every 3 weeks for 45 weeks (15 cycles) • Radiation
No treatment prior to surgery	• Radiation • Chemo every 3 weeks for 9 weeks (3 cycles)	• Radiation

During the study, people will have blood, tumor, urine, and imaging tests, have physical examinations, and answer questions about how they are feeling. After treatment, researchers will follow up with people until the cancer gets better, they are no longer alive, they no longer want to be in the study, or the study ends.

What treatments are being given during the study?

During this study, people will receive standard of care with or without pembrolizumab:

- **Pembrolizumab** given through a vein by intravenous (IV) infusion.
- **Standard of care** including radiation with or without chemotherapy. Chemotherapy is given as an IV infusion.

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

Main goal	How it will be measured
To compare **event free survival** of people who receive pembrolizumab to people who receive standard of care	The length of time people live without the cancer growing, spreading, or coming back
Other goals	**How they will be measured**
To compare **major pathological response** of people who receive pembrolizumab to people who receive standard of care	The number of people whose tumors and lymph nodes removed during surgery have 10% or fewer cancer cells that may be able to spread
To compare **overall survival** of people who receive pembrolizumab to people who receive standard of care	The length of time that people are alive after joining the study
To compare **pathological complete response** of people who receive pembrolizumab to people who receive standard of care	The number of people whose tumors and lymph nodes removed during surgery have no cancer cells that may be able to spread
To compare the **health-related quality of life (HRQoL)** for people who receive pembrolizumab to people who receive standard of care	People will answer sets of questions to measure HRQoL, including: • Overall health • Ability to carry out daily tasks • Ability to swallow and talk • Pain The change in the scores from when the person starts the study until the end of the study will be measured.
To learn about the safety and how well people tolerate pembrolizumab	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 the cancer stop growing or go away after receiving the treatments in this study. This study has a Data Monitoring Committee that oversees the study's overall risk and benefit. If this committee decides that the study treatment is not safe or does not show benefit, the study may be stopped. More information about the benefits and risks for a person may be found in the Investigator's Brochure, Protocol, and Informed Consent documents.