Protocol Plain Language Summary

Clinical study of pembrolizumab with standard treatment in people with bladder cancer (MK-3475-866)

Protocol title: A Phase 3, Randomized, Double-blind Study to Evaluate Perioperative Pembrolizumab (MK-3475) + Neoadjuvant Chemotherapy versus Perioperative Placebo + Neoadjuvant Chemotherapy in Cisplatin-eligible Participants with Muscle-invasive Bladder Cancer (KEYNOTE-866)

Why is this study needed?

Researchers are looking for new ways to treat **muscle-invasive bladder cancer (MIBC)**. MIBC is a type of bladder cancer that spreads to the muscles of the bladder. The **standard treatment** for MIBC is chemotherapy followed by surgery to remove the bladder and lymph nodes around it. **Chemotherapy** is a type of medicine intended to destroy cancer cells or stop them from growing.

In this study, researchers want to learn if people who receive pembrolizumab before surgery with chemotherapy followed by pembrolizumab only after surgery, live longer than people who receive placebo before surgery with chemotherapy followed by placebo only after surgery. **Pembrolizumab (the study medicine)** is an immunotherapy**,** which is a treatment that helps the immune system fight cancer. A **placebo** looks like the study medicine but has no study medicine in it. Using a placebo helps researchers better understand the real effects of the study medicine.

To learn if people live longer, researchers will see if the cancer:

- Grows, spreads, or comes back
- Can be completely removed by surgery

Who will take part in this study?

About 900 people with MIBC will be in this study. They will be ages 18 years and older and:

- Have MIBC that has not spread to other body parts
- Have not been treated for another type of cancer in the past 3 years

What treatments are being given during the study?

Everyone will receive the standard treatment during this study. People will have an equal chance of receiving either:

- **Pembrolizumab**, the study medicine
- **Placebo**

Pembrolizumab and the placebo will be given through a needle into a vein as an infusion once every 3 weeks.

How is this study designed?

This study has 3 parts:

- **Part 1**: People will have an equal chance of receiving pembrolizumab or a placebo for about 3 months before surgery. They will all also receive chemotherapy.
- **Part 2:** People will have surgery to remove their bladder and lymph nodes around it.
- **Part 3**: People will continue receiving pembrolizumab or a placebo based on what they received in Part 1 for about 10 months. They will not receive chemotherapy.

After Part 3, researchers will contact people every 3 months until they leave this study, they are no longer alive, or the study ends. Neither the people in the study nor the researchers will know which treatment a person receives **(double-blind)**. People will 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. People may be in this study for about 6 years.

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

Main goal	How it will be measured
To learn the **event-free survival (EFS)** of people who receive pembrolizumab with chemotherapy before surgery followed by pembrolizumab after surgery compared to people who receive placebo with chemotherapy before surgery followed by placebo after surgery	**EFS** is the length of time that people live from the start of treatment until any of these happen: - Cancer grows, spreads, or comes back - Cancer cannot be removed completely with surgery - Death from any cause
Other goals	**How they will be measured**
To compare the **pathological complete response (pCR)** rate of people who receive pembrolizumab with chemotherapy before surgery to people who receive placebo with chemotherapy before surgery	**pCR** rate is the number of people whose bladders and lymph nodes removed during surgery have no signs of cancer
To compare the **cancer response** in people who receive pembrolizumab with standard treatment to people who receive placebo with standard treatment	During the study, researchers will measure: • **Overall Survival-** the length of time that people live from the start of treatment until death from any cause • **Disease-free Survival-** the length of time that people are cancer free after surgery or death from any cause
To compare the **pathologic downstaging (pDS)** of people who receive pembrolizumab and chemotherapy before surgery to people who receive placebo and chemotherapy before surgery	**pDS** is the number of people whose bladder tumors and lymph nodes which are removed during surgery show that the cancer is not present in the muscle layer of the bladder and lymph nodes around the bladder
To learn about the **safety** and how well people **tolerate** 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 • Had problems around the time of surgery
To compare the **quality of life (QoL)** of people who receive pembrolizumab with standard treatment to people who receive placebo with standard treatment	People will answer questions to measure their **QoL**, including questions about how they are feeling. Researchers will measure: • The change in the scores during the study • The length of time from the start of the study until people's QoL gets worse

What are the possible benefits and risks?

People may or may not benefit from the treatment 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.