Protocol Plain Language Summary

Clinical study of pembrolizumab in combination with chemoradiotherapy in people with muscle invasive bladder cancer (MK-3475-992)

Protocol title: A Phase 3, Randomized, Double-blind, Placebo-controlled Clinical Trial to Study the Efficacy and Safety of Pembrolizumab (MK-3475) in Combination With Chemoradiotherapy (CRT) versus CRT Alone in Participants with Muscle-invasive Bladder Cancer (MIBC) (KEYNOTE-992)

Why is this study needed?

Researchers are looking for new ways to treat muscle-invasive bladder cancer (MIBC). **MIBC** is a type of cancer that has not spread from the muscles in the bladder to other parts of the body.

MIBC is treated by having surgery to remove the bladder (cystectomy). Not all people choose to have surgery and want to keep their bladder using other treatments.

Chemoradiotherapy (CRT) is a non-surgical treatment for MIBC in people that still have their bladder. It combines:

- **Chemotherapy** – a treatment that uses medicine to destroy cancer cells or stop them from growing
- **Radiation therapy** – a treatment that uses beams of intense energy (like X-rays) to shrink or get rid of tumors.

Researchers want to know if **pembrolizumab** given with CRT can help treat MIBC. **Pembrolizumab** is an immunotherapy, which is a treatment that helps the immune system fight cancer**.**

The goal of this study is to learn if pembrolizumab given with CRT can help people live longer without their cancer growing, spreading, or coming back compared to placebo given with CRT. A **placebo** looks like the study medicine but has no study medicine in it. Using a placebo helps researchers better understand if the study medicine works.

Who will take part in this study?

About 636 people with MIBC will be in this study. They will be at least 18 years old and:

- Have a newly found MIBC that has not been treated before
- Can receive CRT
- Have not been treated for another type of cancer in the past 3 years

How is this study designed?

People will have an equal chance of receiving either:

- **Pembrolizumab and CRT**
- **Placebo and CRT**

Neither the people in the study nor the researchers will know which treatment a person receives **(double-blind)**. The study doctor will decide what kind of CRT people will receive.

During the study, 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.

What treatments are being given during the study?

People may be in this study for up to about 7 years.
People will receive one of these through a needle into a vein once every 6 weeks for about 1 year.

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

For **CRT**, everyone will receive:

- Chemotherapy given through a needle in a vein for up to 7 weeks
- Radiation therapy for up to 7 weeks

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

Main goals	How they will be measured
To learn if the **event-free survival (EFS)** of people who receive pembrolizumab and CRT is longer than people who receive placebo and CRT	**EFS** is the length of time people live without the cancer growing, spreading, coming back or surgery to remove the bladder
Other goals	**How they will be measured**
To learn if the **overall survival (OS)** of people who receive pembrolizumab and CRT is longer than people who receive placebo and CRT	**OS** is the length of time that people live from the start of the study until death from any cause
To learn if the **metastasis-free survival (MFS)** of people who receive pembrolizumab and CRT is longer than people who receive placebo and CRT	**MFS** is the length of time from the when the person starts the study until either the cancer spreads from where it started to other parts of the body, or death from any cause
To learn if pembrolizumab and CRT or placebo and CRT delay the **time** the **non-muscle-invasive bladder cancer (NMIBC)** is found	**Time to NMIBC** is the length of time people live from the start of the study until researchers find NMIBC (cancer that has not spread past the inner layer of the bladder)
To learn if pembrolizumab and CRT or placebo and CRT delay the **time to bladder removal**	**Time to bladder removal** is the length of time people live from the start of the study until they have surgery to remove their bladder
To learn about the **safety** and how well people **tolerate** pembrolizumab and **CRT**	The number of people who: • Had an **adverse event (AE)** An AE is a health problem that happens or worsens during the study • Stopped treatment due to an AE
To learn about the **health-related quality of life (HRQoL)** of people who receive pembrolizumab and CRT compared to those who receive placebo and CRT	People will answer questions to measure their **HRQoL** including questions about their overall health and the ability to carry out daily tasks. Researchers will measure the change in the scores during the study.

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 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.