Protocol Plain Language Summary

A clinical study of enfortumab vedotin and pembrolizumab compared to chemotherapy to treat muscle invasive bladder cancer (MK-3475-B15)

Protocol title: A Phase 3, Randomized, Open-label Study to Evaluate Perioperative Enfortumab Vedotin Plus Pembrolizumab (MK-3475) Versus Neoadjuvant Gemcitabine and Cisplatin in Cisplatin-eligible Participants with Muscle-invasive Bladder Cancer (KEYNOTE-B15 / EV-304)

Why is this study needed?

Researchers are looking for new ways to treat muscle-invasive bladder cancer (MIBC). **MIBC** is cancer in the bladder muscles that has not spread outside of the bladder.

Standard treatment for MIBC is **chemotherapy** followed by **surgery** to remove the bladder and nearby **lymph nodes**. Chemotherapy is a treatment that uses medicine to destroy cancer cells or stop them from growing. A **lymph node** is a small, bean-shaped organ that is part of the immune system.

Researchers want to know if giving **enfortumab vedotin (EV)** and **pembrolizumab** before and after surgery can treat MIBC. **EV** is a targeted therapy, which works on specific cancer cells to stop them from growing. **Pembrolizumab** is an immunotherapy, which is a treatment that helps the immune system fight cancer**.**

The goal of this study is to learn if people who receive EV and pembrolizumab live longer without the cancer growing, spreading, or coming back than people who receive standard treatment.

Who will take part in this study?

About 784 people with MIBC will be in this study. They will be at least 18 years old and:

- Can have surgery to remove the bladder and nearby lymph nodes
- Have not been treated for MIBC before
- Have not been treated for another type of cancer in the past 3 years

What treatments are being given during the study?

All people will have surgery and receive 1 or 2 of these treatments:

- **Enfortumab vedotin (EV)**, the study medicine
- **Pembrolizumab**, the study medicine
- **Chemotherapy**

People will receive their treatment once or twice every 3 weeks through a needle into a vein as an intravenous (IV) infusion.

How is this study designed?

People will be assigned to one of these groups:

	Treatment before surgery	**Treatment after surgery**
Group A	**EV and pembrolizumab** for about 2 and a half months	People who have no signs of cancer (based on imaging tests) will receive **EV** for about 3 and a half months and **pembrolizumab** for about 9 months
Group B	**Chemotherapy** for about 2 and half months	Researchers may decide to give some people an immunotherapy after surgery

Both the people in the study and the researcher will know which study treatment a person is getting (open-label 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, bladder cancer symptoms, and their ability to carry out daily tasks.

Researchers will follow people until they leave the study, the study ends, or death from any cause. People may be in this study for about 5 and a half years.

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 (EFS)** for people in Groups A and B	**EFS** is the length of time from when the person starts the study until any of these happen: • They could not have surgery because the cancer got worse or could not be removed • The surgery could not remove all the cancer • The cancer comes back after surgery • Death from any cause
Other goals	**How they will be measured**
To compare **pathological complete response (pCR)** for people in Groups A and B	pCR is the number of people whose bladder and lymph nodes removed during surgery have no signs of cancer
To compare **overall survival (OS)** for people in Groups A and B	**OS** is the length of time from when the person starts the study until death from any cause
To learn about the **disease-free survival (DFS)** for people in Groups A and B who have no signs of cancer after surgery	**DFS** is the length of time that people are cancer free after surgery
To learn about the **pathological downstaging (pDS)** for people in Groups A and B	**pDS** is the number of people whose bladder cancer has gotten smaller or have no signs of cancer after surgery
To learn about the **safety** and how well people **tolerate** the treatments in Group A	The number of people who: • Have an **adverse event (AE).** An AE is a health problem that happens or worsens during a study • Stop treatment due to an AE • Have medical problems during surgery
To learn about the change in **health-related quality of life (HRQoL)** for people in Groups A and B	People will answer questions to measure their **HRQoL**. Researchers will measure the change in scores from when the person starts the study until the end of the study. The questions are about their overall health, ability to carry out daily tasks, and bladder cancer symptoms

What are the possible benefits and risks?

People may or may not benefit from the treatment received during the study. The 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 Protocol.