Clinical study of pembrolizumab plus enzalutamide in men with metastatic prostate cancer (MK-3475-641)

Protocol title: A Phase 3, Randomized, Double-blind Trial of Pembrolizumab (MK-3475) Plus Enzalutamide Versus Placebo Plus Enzalutamide in Participants With Metastatic Castration-Resistant Prostate Cancer (mCRPC) (KEYNOTE-641)

Why is this study needed?

Researchers are looking for new ways to treat metastatic castration-resistant prostate cancer (mCRPC). **mCRPC** is a type of prostate cancer that has metastasized (spread) to other parts of the body and got worse or came back after treatment to lower testosterone (a hormone). The prostate is a small walnut sized gland that produces the fluid that transports sperm.

Standard treatment for mCRPC is **enzalutamide**, which is an anti-hormone therapy (treatment that blocks or lowers hormones that can help cancer grow). **Pembrolizumab** is an immunotherapy, which is a treatment that helps the immune system fight cancer.

The goal of this study is to learn if taking pembrolizumab with enzalutamide can help people live longer compared to people taking placebo with enzalutamide. Researchers also want to learn if people taking pembrolizumab with enzalutamide live longer without the cancer getting worse compared to people taking placebo with enzalutamide.

Who will take part in this study?

About 1,240 men with mCRPC will be in this study. They will be ages 18 years and older and have:

- Prostate cancer get worse while on ADT (androgen deprivation therapy) or after surgery to remove their testicles
- Not been treated for another type of cancer in the past 3 years

What treatments are being given during the study?

All people in this study will take **enzalutamide** (standard treatment) as pills by mouth once a day until their cancer gets worse.

People will also receive one of these through a needle in a vein (called an intravenous, or IV, infusion) once every 3 weeks for up to about 2 years:

- **Pembrolizumab**, which is the study medicine
- **Placebo,** which looks like the study medicine but does not have any medicine in it. Using a placebo helps researchers better understand the real effects of the study medicine.

If treatment works for a person, they may be able to receive treatment for up to one more year.

Most people have stopped receiving pembrolizumab. People who cannot access enzalutamide may stay on this treatment with researcher approval.

How is this study designed?

People will have an equal chance of being assigned to one of these treatment groups:

- **Pembrolizumab and enzalutamide**
- **Placebo and enzalutamide**

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

During the study, people may have biopsies (tumor and bone), blood, urine and imaging tests, physical examinations, and answer questions about how they are feeling. After people finish treatment, researchers will contact them about every 3 months until they leave the study, the study ends or death. People may be in this study for up to about 5 and a half years.

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

Main goals	How they will be measured
To learn if the **overall survival (OS)** of people who receive pembrolizumab and enzalutamide is longer than people who receive placebo and enzalutamide	**OS** is the average length of time that people live from the start of treatment until death from any cause
To learn if the **radiographic progression-free survival (rPFS)** of people who receive pembrolizumab and enzalutamide is longer than people who receive placebo and enzalutamide	**rPFS** is the average length of time from the start of treatment until cancer grows or spreads (based on imaging tests), or death from any cause
Other goals	**How they will be measured**
To learn about the **time to the next treatment or death(TFST)** of people who receive pembrolizumab and enzalutamide compared to people who receive placebo and enzalutamide	**TFST** is the average length of time from the start of treatment until the start of a new cancer treatment or death
To learn about the **levels of prostate specific antigen (PSA)** in people who receive pembrolizumab and enzalutamide compared to people who receive placebo and enzalutamide. **PSA** is a protein made by the prostate that is	During the study, researchers will do blood tests to measure: • **PSA response**: the percent of people who have a PSA level go down by at least half 2 times 3-weeks apart • **PSA undetectable**: the percent of people whose PSA is too low to be measured

in the blood. It may be higher in people with prostate cancer.	• **PSA progression**: the average length of time from the start of treatment until the PSA goes up by a certain level
To learn about the **cancer response** of people who receive pembrolizumab and enzalutamide compared to people who receive placebo and enzalutamide	During the study, researchers will measure: • **Objective response rate (ORR)**: the number of people whose cancer responds to treatment (gets smaller or goes away) • **Duration of response (DOR)**: the length of time from when the cancer first responds to treatment until the cancer grows, spreads, or death from any cause • **Radiographic soft-tissue progression**: the length of time from the start of treatment until the cancer spreads to soft tissue (muscle, fat, blood vessels, or other tissue)
To learn about the **pain and bone health** of people who receive pembrolizumab and enzalutamide compared to people who receive placebo and enzalutamide	During the study, the researchers will measure the length of time from the start of treatment until: • A person's pain worsens by a certain amount called **time to pain progression (TTPP)** • Certain bone-related events happen called **symptomatic skeletal-related event (SSRE)**, such as certain treatments, surgeries, or broken bones
To learn about the safety of pembrolizumab and enzalutamide and how well people tolerate it	During the study, the number of people who: • Had an **adverse event (AE)** – an AE is a health problem that happens or worsens during a study • Stopped treatment due to an AE

What are the possible benefits and risks?

People in this study may or may not have their cancer stop growing or go away. This study has an external group of experts that will oversee the overall risk and benefit. After a planned review, the sponsor has decided not to continue the study except for people who may be receiving benefit from the study treatment.

More information about the benefits and risks is in the Investigator Brochure, Protocol, and Informed Consent documents.