Protocol Plain Language Summary

A clinical study of belzutifan to prevent kidney cancer from coming back after surgery (MK-6482-022)

Protocol Title: A Multicenter, Double-blind, Randomized Phase 3 Study to Compare the Efficacy and Safety of Belzutifan (MK-6482) Plus Pembrolizumab (MK-3475) Versus Placebo Plus Pembrolizumab, in the Adjuvant Treatment of Clear Cell Renal Cell Carcinoma (ccRCC) Post Nephrectomy (MK-6482-022)

Why is this study needed?

Researchers are looking for new ways to prevent kidney cancer called **renal cell carcinoma (RCC)** from coming back after a person had surgery to remove the cancer. **Belzutifan**, also called MK-6482, is a study medicine designed to block a protein that helps tumors grow and survive. **Pembrolizumab** is an immunotherapy which is a treatment that helps the immune system fight cancer.

Researchers want to learn if people who are treated with belzutifan and pembrolizumab live longer without the cancer coming back than people who are treated with pembrolizumab alone.

Who will take part in this study?

About 1800 people will take part in this study. They will be at least 18 years old and:

- Have clear cell RCC (most common type of RCC)
- Had surgery to remove the RCC in the past 3 months
- Have not had treatment for RCC (except the surgery)
- Do not need to be treated with oxygen

What treatments are being given during the study?

Everyone will receive pembrolizumab every 6 weeks through a needle in a vein as an intravenous (IV) infusion. People will also take either:

- Belzutifan once a day by mouth as tablets
- Placebo once a day by mouth as tablets. A placebo looks like the study medicine but has no study medicine in it. Using a placebo helps researchers better understand the effects of a study medicine.

A person will be treated for about a year unless the cancer returns or the person doesn't tolerate treatment.

How is this study designed?

A person may be in this study for up to about 8 years. Within 3 months of the surgery for RCC, people will have an equal chance of being assigned to either:

- Belzutifan and pembrolizumab
- Placebo and pembrolizumab

Neither the people in the study nor the researcher will know which study treatment a person is getting (**double-blind study**). During the study, people will give urine and blood samples, have imaging tests, physical examinations, and answer questions about how they are feeling and their ability to carry out daily tasks.

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

Main goal	How it will be measured
To learn if people who receive belzutifan and pembrolizumab have a longer **disease-free survival (DFS)** than people who receive pembrolizumab alone	DFS is the length of time that people are cancer free after starting in the study
Other goals	**How they will be measured**
To learn if the **overall survival (OS)** of people who receive belzutifan and pembrolizumab is longer than people who receive pembrolizumab alone	OS is the length of time that people live from starting in the study until death from any cause
To learn about the **safety** and how well people **tolerate** belzutifan and pembrolizumab compared to pembrolizumab alone	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
To learn if people who receive belzutifan and pembrolizumab have longer **disease recurrence-specific survival (DRSS)** compared to people who receive pembrolizumab alone	Researchers will measure the length of time from when the person starts the study until: • Cancer comes back to where it first started • Cancer comes back to where it first started or spreads to other parts of the body (whichever happens first)
To compare the **health-related quality of life (HRQoL)** for people who receive belzutifan and pembrolizumab to people who receive pembrolizumab alone	People will answer sets of questions to measure HRQoL, including questions about: • Overall health • Ability to carry out daily tasks • Ability to carry out other daily activities such as work or hobbies • Certain symptoms that happen if cancer returns The change in the scores from when the person starts the study will be measured up to about 3 years.

What are the possible benefits and risks?

People in this study 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 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 for a person may be found in the Investigator's Brochure, Protocol, and Informed Consent documents.