Protocol Plain Language Summary

A clinical study of belzutifan in people with advanced kidney cancer (MK-6482-005)

Protocol Title: An Open-label, Randomized Phase 3 Study of MK-6482 Versus Everolimus in Participants with Advanced Renal Cell Carcinoma That Has Progressed After Prior PD 1/L1 and VEGF-Targeted Therapies

Why is this study needed?

Researchers are looking for more ways to treat advanced **renal cell carcinoma (RCC).** RCC is the most common type of kidney cancer. **Advanced** means cancer cannot be removed with surgery or has spread to other parts of the body.

Researchers want to learn if belzutifan, also called MK-6482, can help treat advanced RCC. **Belzutifan** is a study medicine designed to block a protein that helps tumors grow and survive.

The goal of this study is to learn if people who receive belzutifan live longer overall and without the cancer getting worse than people who receive everolimus. **Everolimus** is a medicine that blocks a different protein that helps tumors grow and survive.

Who will take part in this study?

About 736 people with advanced RCC will be in the study. They will be at least 18 years old and:

- Had the cancer get worse during or after certain treatments
- Have not had the cancer spread to their brain or spine

What treatments are being given during the study?

People will have an equal chance of taking one of these treatments:

- **Belzutifan**, the study treatment
- **Everolimus**

People will take their treatment by mouth as tablets once a day. They will take it until their cancer gets worse, the person or their study doctor decides to end treatment, or the study ends. There may be certain other reasons a person stops study treatment.

How is this study designed?

Both the people in the study and the researcher will know which study treatment a person is getting (**open-label study**). During the study, people will give blood, urine, and tumor samples, have imaging tests and physical examinations, and answer questions about their health.

A person may be in this study for up to 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 about the **cancer response** of people who receive belzutifan compared to people who receive everolimus	Researchers will measure: • **Progression free survival:** the length of time from when the person starts in the study until the cancer grows or spreads, or death from any cause • **Overall survival:** the length of time that people live from the start of the study until death from any cause
Other goals	**How they will be measured**
To learn **more about the cancer response** of people who receive belzutifan compared to people who receive everolimus	Researchers will measure: • **Overall response:** the number of people whose cancer responds to treatment (gets smaller or goes away) during the study. • **Duration of response:** the length of time from when the cancer first responds to treatment until the cancer grows, spreads, or death from any cause
To learn about the **safety** of belzutifan and how well people **tolerate** it compared to everolimus	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
To learn about the **health-related quality of life (HRQoL)** of people who receive belzutifan compared to people who receive everolimus	People will answer sets of questions to measure their HRQoL, including questions about their overall health and their ability to carry out daily tasks. The change in the scores will be measured during the study.

What are the possible benefits and risks?

Clinical studies may have benefits and risks. People may benefit because the study medicine may treat cancer or stop it from getting worse. There may be risks because the study medicine may not work or may cause health problems.

This study has a group of experts, separate from the researchers, who oversee the benefits and risks. If they decide that the study medicine is not safe or doesn't show benefit, the study can be stopped. More information about the benefits and risks is in the protocol.