

## A study of belzutifan with palbociclib for the treatment of kidney cancer (MK-6482-024)

**Protocol Title:** A Multicenter, Open-label, Randomized, Phase 1/2 Study of Belzutifan in Combination with Palbociclib Versus Belzutifan Monotherapy in Participants with Advanced Renal Cell Carcinoma

### Why is this study needed?

Researchers are looking for new ways to treat a type of kidney cancer called advanced **renal cell carcinoma (RCC)**. Advanced means cancer has spread to other parts of the body or cannot be removed with surgery. **Belzutifan**, also called MK-6482, is a study medicine designed to block a protein that helps tumors grow and survive. **Palbociclib** is a type of targeted therapy. A targeted therapy is a type of treatment that works on proteins that control how specific cancer cells grow and spread.

Researchers want to learn about:

- The safety of belzutifan alone or with palbociclib and how well people tolerate it
- The dose level (amount) of belzutifan to give with palbociclib
- How the cancer responds to treatment

### Who will take part in this study?

About 180 people with advanced RCC will take part in this study. They will be ages 18 and older and:

- Have received at least 2 certain types of treatment for advanced clear cell RCC (the most common type of RCC)
- Had cancer get worse during or after most recent treatment for RCC
- Do not need to be treated with oxygen
- Are able to swallow the study pills

### What treatments are being given during the study?

People will take belzutifan alone or with palbociclib by mouth as tablets:

- Belzutifan once a day
- Palbociclib, at different dose levels once a day for 3 weeks. They will stop palbociclib for 1 week. This will be repeated while the person is in the study.

### How is this study designed?

A person may be in this study for up to about 5 years. This study has 2 parts.

**Part 1:** about 30 people will take belzutifan once a day and palbociclib at different dose levels once a day for 3 out of 4 weeks. Researchers will start by giving up to 10 people the lowest dose of palbociclib. They will check to see if there are any safety concerns during the first 4 weeks before giving the next group a higher dose. This will help the researchers find the **recommended dose** of palbociclib to give during part 2 of the study.

**Part 2:** About 150 people will take either:

- Belzutifan once a day and palbociclib once a day for 3 out of every 4 weeks
- Belzutifan alone once a day

People will have a 2 in 3 chance (66%) of taking belzutifan with palbociclib and a 1 in 3 chance (33%) of taking belzutifan alone. All people will take treatment until the cancer gets worse, they don't tolerate it, or they decide to stop taking part in the study.

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 urine and blood samples, have tumor imaging tests, and physical examinations.

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

Main goals	How they will be measured
<b>Part 1:</b> To learn about the <b>safety</b> of belzutifan with palbociclib and how well people <b>tolerate</b> it	During Part 1, the number of people who: <ul style="list-style-type: none"> <li>• Had an <b>adverse event (AE)</b> – an AE is a health problem that happens or worsens</li> <li>• Stopped treatment due to an AE</li> <li>• Had a <b>dose limiting toxicity (DLT)</b> – a DLT is a health problem (AE) related to treatment that prevents giving a higher dose or may prevent giving the same dose</li> </ul>
<b>Part 2:</b> To learn about the <b>objective response</b> to treatment	During Part 2, researchers will measure the <b>objective response rate (ORR)</b> . ORR is the number (percent) of people whose cancer responds to treatment (gets smaller or goes away)
Other goals	How they will be measured
<b>Part 2:</b> To learn the <b>cancer response</b> to belzutifan alone or with palbociclib	During Part 2, researchers will measure: <ul style="list-style-type: none"> <li>• <b>Clinical benefit rate:</b> the number (percent) of people whose cancer stays the same for at least 6 months or the cancer gets smaller or goes away</li> <li>• <b>Duration of response:</b> the length of time from when the cancer first responds to treatment until the cancer grows, spreads, or death from any cause</li> <li>• <b>Progression free survival:</b> the length of time from the start of treatment until the cancer grows or spreads, or death from any cause</li> <li>• <b>Overall survival:</b> the length of time that people live from the start of treatment until death from any cause</li> </ul>
<b>Part 2:</b> To learn about the <b>safety</b> of belzutifan alone or with palbociclib and how well people <b>tolerate</b> it	During Part 2, the number of people who: <ul style="list-style-type: none"> <li>• Had an AE</li> <li>• Stopped treatment due to an AE</li> </ul>

### What are the possible benefits and risks?

People in this study may or may not benefit from the treatment received during the study. More information about the benefits and risks for a person is in the protocol.