# Clinical Study Results

This summary reports the results of only one study. Researchers must look at the results of many types of studies to understand if a study medication works, how it works, and if it is safe to prescribe to study participants. The results of this study might be different than the results of other studies that the researchers review.

**Sponsor:** Pfizer Inc.

**Medicine(s) Studied:** Axitinib (AG-013736)

**Protocol Number:** A4061079

**Dates of Study:** 16 September 2014 to 03 July 2019

**Title of this Study:** Study to Evaluate Safety of Axitinib in Combination with MK-3475 in Patients with Advanced Renal Cell Cancer.

[A phase 1b, open label, dose finding study to evaluate safety, pharmacokinetics and pharmacodynamics of Axitinib (AG-013736) in combination with Pembrolizumab (MK-3475) in patients with advanced renal cell cancer]

**Date(s) of this Report:** 19 April 2021

## – Thank You –

If you participated in this study, Pfizer, the Sponsor, would like to thank you for your participation.

This summary will describe the study results. If you have any questions about the study or the results, please contact the doctor or staff at your study site.

# Why was this study done?

## What is Advanced Renal Cell Cancer?

Cancer occurs when cells in the body divide without control and can spread to other parts of the body. Renal cell cancer is the most common form of kidney cancer. It starts in the lining of the small tubes inside the kidney that help clean and filter blood. Advanced renal cell cancer is when the disease has progressed to Stage IV and has spread to other parts of the body.

## What are Axitinib and MK-3475?

Axitinib, pronounced AK-sih-TIH-nib, also called Inlyta®, is a tablet, taken by mouth twice a day. Researchers think Axitinib may help patients with advanced renal cell cancer by stopping the body from making a protein called "vascular endothelial growth factor", or VEGF. Cancer cells make extra amounts of some proteins including VEGF when growing. The extra VEGF tells the surrounding cells to make new blood vessels that tumors need to grow. Blood vessels are tiny tubes that allow blood to move around and provide nutrients and oxygen to all the parts of the body.

MK-3475, also called Pembrolizumab or Keytruda®, is an intravenous (IV) treatment that researchers believe may help patients with cancer. MK-3475 works by sticking to a protein called "anti-programmed cell death protein", which prevents it from protecting cancer cells from the body's immune system.

Researchers think taking both Axitinib and MK-3475 may help patients with advanced renal cell cancer, as they work in different ways. However, first they needed to know more about the safety of taking both these treatments at the same time.

## What was the purpose of this study?

The purpose of this study was to and learn how safe the combination of Axitinib MK-3475 were for patients with advanced renal cell cancer and figure out the best dose to use in future studies.

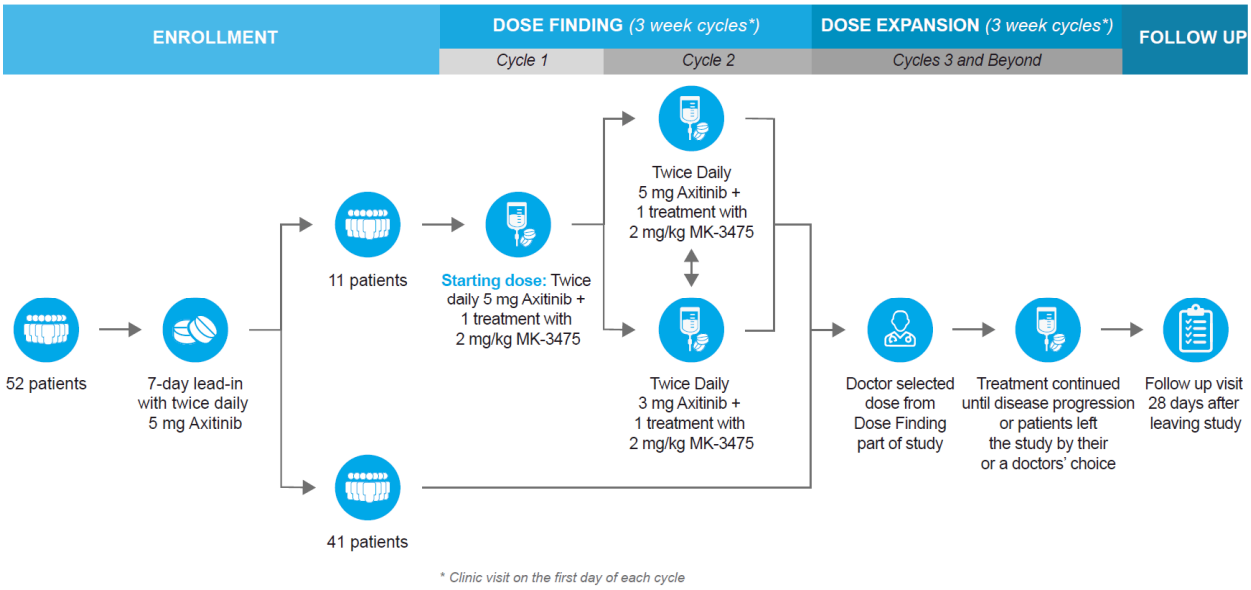
## Researchers wanted to know:

- **How safe was the combination of Axitinib and MK-3475 for participants with advanced renal cell cancer?**
- **What medical problems did participants have during the study?**

# What happened during the study?

## How was the study done?

This study had two parts: the dose finding part and the *dose expansion* part.



Researchers tested 2 different doses of Axitinib in combination with 2 milligrams per kilogram each participant weighed (also called "mg/kg") of MK-3475 on a group of participants with advanced renal cell cancer to learn how safe the combination of Axitinib and MK-3475.

In the dose finding part of the study, participants were to take Axitinib at a dose of 5 mg by mouth, twice a day. Participants were also to take 2 mg/kg MK-3475 inside the vein (IV). After 3 weeks, the participants either continued taking the 5 mg dose of Axitinib or were switched to the 3 mg dose of Axitinib.

The participants and researchers knew who took the 5 mg dose of Axitinib and who took 3 mg dose of Axitinib. All participants knew they were taking MK-3475. This is known as an "open-label" study. Participants were assigned to each group by their doctor based on each participant's condition.

During the dose expansion part of the study, the participants from the dose finding part of the study continued to take these medications at the dose chosen by their doctors. New patients also joined the study and were given 1 of the 2 doses of Axitinib as chosen by their doctors.

Researchers took samples of blood and urine from participants once every 3 weeks during both the dose finding and *dose expansion* parts of the study and measured the amounts of Axitinib and MK-3475. Researchers also checked the participants' health during the study and asked them how they were feeling.

Researchers then compared the number of participants that had certain medical problems in the Axitinib 5 mg to the participants taking Axitinib 3 mg.

## Where did this study take place?

The Sponsor ran this study at 10 locations in 1 country in North America.

## When did this study take place?

It began 16 September 2014 and ended 03 July 2019.

## Who participated in this study?

The study included participants who were at least 18 years old, had advanced renal cell cancer, and at least 1 tumour their doctor could measure.

A total of 41 men participated
A total of 11 women participated
All participants were between the ages of 28 and 75 years

Participants were to be treated until their cancer got worse, they chose to leave the study, or a doctor decided it was best for them to stop being in the study. Of the 52 participants who started the study, no patients were still continuing in the study at the time of this report.

## How long did the study last?

The amount of time that study participants were in the study varied depending on their response to the study treatment, but the entire study took 58 months to complete.

When the study ended in July 2019, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

# What were the results of the study?

## Were there any safety concerns for participants taking Axitinib in combination with MK-3475?

To learn more about safety, the study doctors did a number of tests and exams, including lab tests, heart tracings, physical exams, and vital signs (blood pressure, weight, and heart rate). There were no meaningful changes found on these tests.

The researchers also examined what medical problems the patients experienced during the study. This information is provided in the next section.

This does not mean that everyone in this study had these results. Other studies may produce different results, as well. These are just some of the main findings of the study, and more information may be available at the websites listed at the end of this summary.

## What medical problems did participants have during the study?

The researchers recorded any medical problems the participants had during the study. Participants could have had medical problems for reasons not related to the study (for example, caused by an underlying disease or by chance). Or, medical problems could also have been caused by a study treatment or by another medicine the participant was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many treatment groups in many studies, doctors try to understand what effects a study medication might have on a participant.

All 52 (100%) participants in this study had at least 1 medical problem. A total of 20 (20% or 1 out of 5) participants left the study because of medical problems. The most common medical problems – those reported by at least 20% of participants – are described below.

Below are instructions on how to read Table 1.

**Instructions for Understanding Table 1.**

- The **1st** column of Table 1 lists medical problems that were commonly reported during the study. All medical problems reported by at least 20% of participants are listed.
- The **2nd** column tells how many of the 52 participants reported each medical problem that the researchers felt were due to either of the study medications. Next to this number is the percentage of the 52 participants who reported the medical problem.
- Using these instructions, you can see that 39 out of the 52 participants taking the study medications reported feeling tired.

## Table 1. Commonly reported medical problems by at least 20% of study participants

| Medical Problem | Axitinib or MK-3475 (All 52 Participants) |
|---|---|
| Feeling tired | 39 out of 52 participants (75%) |
| Loose stools | 38 out of 52 participants (73%) |
| High blood pressure | 26 out of 52 participants (50%) |
| Difficulty speaking | 24 out of 52 participants (46%) |
| ALT liver test levels increased | 20 out of 52 participants (39%) |
| Decreased appetite | 19 out of 52 participants (37%) |
| Low levels of thyroid hormone | 19 out of 52 participants (37%) |
| Nausea | 19 out of 52 participants (37%) |
| Hand-foot syndrome | 19 out of 52 participants (37%) |
| AST liver test levels increased | 16 out of 52 participants (31%) |
| High levels of protein in urine | 15 out of 52 participants (29%) |
| Weight loss | 15 out of 52 participants (29%) |
| Joint pain | 12 out of 52 participants (23%) |
| Headache | 12 out of 52 participants (23%) |
| Oral pain | 12 out of 52 participants (23%) |
| Abdominal pain | 11 out of 52 participants (21%) |

# Did study participants have any serious medical problems?

A medical problem is considered "serious" when it is life-threatening, needs hospital care, or causes lasting problems.

Twenty-nine (29) participants (56%, or 14 out of 25 participants) had serious medical problems while taking Axitinib and MK-3475. Serious medical problems reported by at least 2% of study participants can be found in Table 2, below.

Fourteen (14) patients died during the study, 11 were due to their cancer getting worse, 2 were due to unknown causes, and 1 death happened from a medical procedure. Only 1 death occurred while the participant was taking the study medications, the other 13 deaths were more than 90 days after the participants had received their last dose. The researchers did not consider these deaths to be related to the study medicines.

**Table 2. Serious medical problems reported by at least 2% of study participants**

| Medical Problem | Axitinib or MK-3475 (All 52 Participants) |
|---|---|
| **Loose stools** | 6 out of 52 participants (12%) |
| **Shortness of breath** | 4 out of 52 participants (8%) |
| **ALT liver test increased** | 3 out of 52 participants (6%) |
| **Inflammation of the colitis** | 3 out of 52 participants (6%) |
| **Feeling tired** | 2 out of 52 participants (4%) |
| **Fluid between the lungs and chest** | 2 out of 52 participants (4%) |
| **Blocked small intestines** | 2 out of 52 participants (4%) |
| **Vomiting** | 2 out of 52 participants (4%) |

## Where can I learn more about this study?

If you have questions about the results of your study, please speak with the doctor or staff at your study site.

For more details on your study protocol, please visit:

The full scientific report of this study is available online at:

| | |
|---|---|
| www.clinicaltrials.gov | Use the study identifier **NCT02133742** |
| www.pfizer.com/research/research_clinical_trials/trial_results | Use the protocol number **A4061079** |

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for study participants.

Again, if you participated in this study,
**thank you** for volunteering.
We do research to try to find the
best ways to help study participants, and you
helped us to do that!