Clinical Study Results

AstraZeneca

Research Sponsor: AstraZeneca

Drug Studied: Savolitinib, also called volitinib and AZD6094

Study Title: A study to learn if savolitinib slows cancer growth compared to sunitinib in participants with advanced papillary kidney cancer

Thank you!

Thank you for taking part in the clinical study for the study drug savolitinib, also called AZD6094. You and all of the participants helped researchers learn more about savolitinib to help people with a type of kidney cancer called papillary renal cell carcinoma. This cancer is also called PRCC.

AstraZeneca sponsored this study and thinks it is important to share the results of the study with you and the public. An independent non-profit organization called CISCRP helped prepare this summary of the study results for you. We hope it helps you understand and feel proud of your important role in medical research.

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

What is happening with the study now?

The participants were in the study for up to about 2 years. The study started in July 2017 and ended in August 2019. The researchers planned to include 180 participants in the study, but the study was closed early. This was because results from another study in people with PRCC suggested that this new type of treatment may not affect this type of cancer any differently than existing treatments.

This study included 60 participants in Brazil, France, Italy, the Republic of Korea, Russia, Ukraine, and the United States.

The sponsor reviewed the data collected when the study ended and created a report of the results. This is a summary of that report.

Why was the research needed?

Researchers are looking for a better way to treat patients who have advanced PRCC. “Advanced” means that the cancer has spread from where it started to other parts of the body and cannot be treated with surgery. Before a drug can be approved for patients to take, researchers do clinical studies to find out how safe it is and how it works.

In this study, the researchers wanted to find out how well savolitinib works compared to sunitinib in participants with advanced PRCC. Sunitinib is a drug that is often used to treat this type of cancer. The researchers also wanted to find out if the participants had any medical problems during the study.

PRCC is a kidney cancer that can be caused by changes in the DNA of different genes. There are treatments for kidney cancers, but none of these were developed to treat PRCC specifically.

Savolitinib was developed to slow the growth of tumor cells with changes in a gene called the MET gene. Research has shown that changes in the DNA of the MET gene can make PRCC tumors grow faster.

In this study, the researchers wanted to find out if savolitinib slowed tumor growth compared to sunitinib in participants with PRCC that had changes in the MET gene. The researchers compared savolitinib with the kidney cancer drug sunitinib.

The main questions the researchers wanted to answer in this study were:

- Did savolitinib slow the participants’ tumor growth compared to sunitinib?
- Did the participants’ quality of life change after taking study treatment?
- What medical problems did the participants have during the study?

To answer the questions in this study, the researchers asked for the help of men and women with advanced PRCC that had been caused by a change in the MET gene. They had never taken sunitinib before or any treatment that works in the same way as savolitinib. The participants in this study were 23 to 78 years old.

What kind of study was this?

This was an “open-label” study. This means the researchers and the participant knew what the participant was taking.

In this study, the participants took savolitinib or sunitinib as a pill by mouth. The doses were measured in milligrams, also called mg.

There were 2 treatment groups in this study. A computer program was used to randomly choose the treatment each participant took. This helps make sure the groups are chosen fairly. Researchers do this so that comparing the results of each treatment is as accurate as possible.

In this study, the participants took study treatment in 6-week time periods called “cycles”. The participants could keep taking study treatment until one of these happened:

- their cancer got worse
- they had a medical problem that the doctors thought might be related to the study treatment
- they wanted to leave the study

The table below shows the treatments in this study.

Group	Treatment	Treatment schedule each cycle
Group 1 (33 participants)	600 mg of savolitinib	Once a day for 6 weeks
Group 2 (27 participants)	50 mg of sunitinib	Once a day for 4 weeks, then no treatment for 2 weeks

What happened during the study?

Before the participants took any study treatment, the doctors checked their overall health to make sure that they could join the study. The doctors:

- took blood and urine samples
- took pictures of the participants' tumors using CT, MRI scans, or both
- took samples of the participants' tumors to test for changes in the MET gene

While the participants were taking study treatment, they visited their study site a total of 5 times during the first 2 treatment cycles. After this, the participants visited the study site 1 time at the start of each new treatment cycle. At these visits, the doctors took blood samples and checked the participants' health.

During the study, the doctors:

- took pictures of the participants' tumors using CT and/or MRI scans every 6 weeks
- gave the participants surveys about their quality of life every 2 or 4 weeks

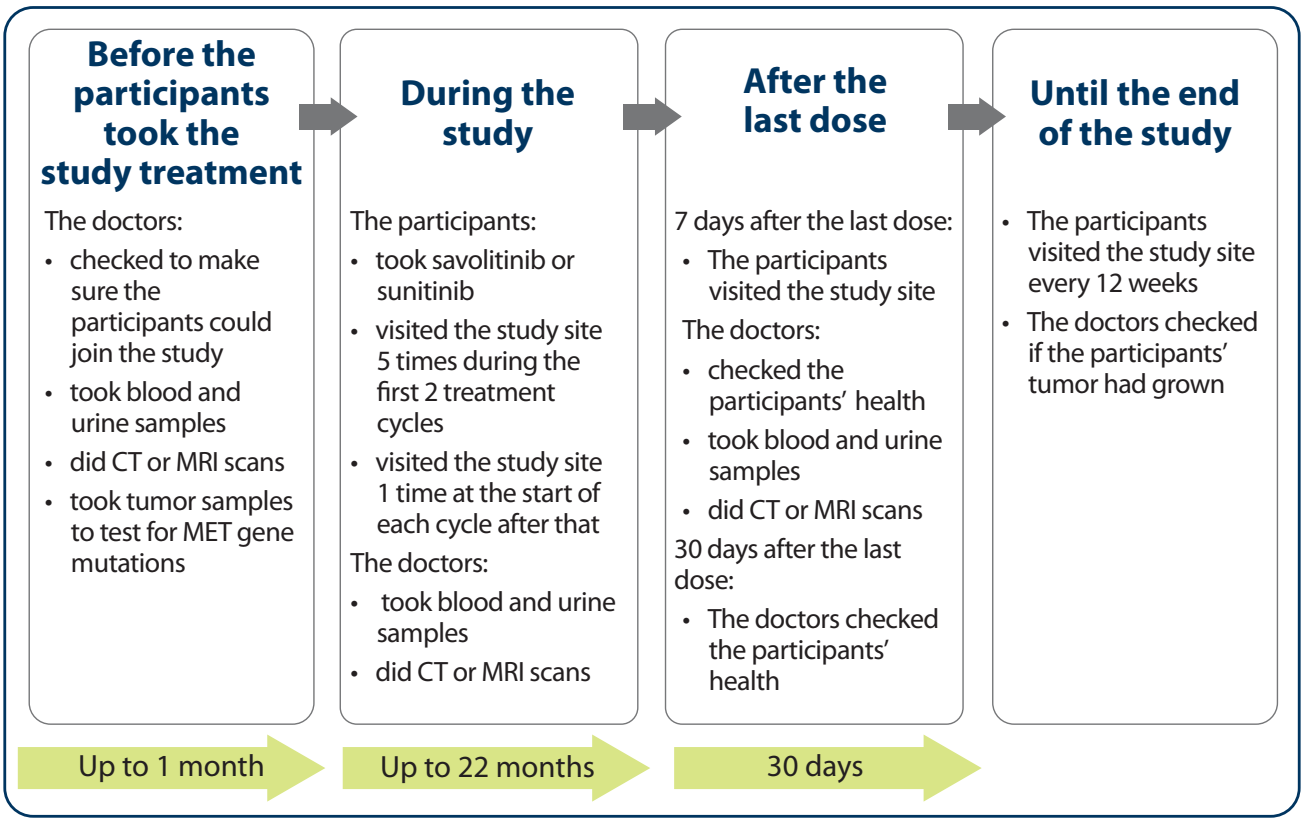
About 7 days after the last dose, the participants visited the study site. At this visit, the doctors:

- checked the participants' health
- took blood and urine samples
- took pictures of the participants' tumors using CT, MRI scans, or both

Some participants could keep taking study treatment after the last planned dose, if the study doctor agreed it was helping them.

About 30 days after the last dose, the doctors checked the participants' health. This could be done over the phone or at a visit to the study site.

After this, the participants visited the study site every 12 weeks for as long as they stayed in the study. At these visits, the doctors took pictures of the participants' tumors using CT or MRI scans.



What were the results of the study?

This is a summary of the main results from this study overall. The results each participant had might be different and are not in this summary. A full list of the questions researchers wanted to answer can be found on the websites listed at the end of this summary. If a full report of the study results is available, it can also be found on these websites.

Researchers look at the results of many studies to decide which treatments work best and are safest. Other studies may provide new information or different results. Always talk to a doctor before making any treatment changes.

Did savolitinib slow the participants' tumor growth compared to sunitinib?

Overall, the difference between the treatment groups was too small for the researchers to know if savolitinib slowed the participants' tumor growth compared to sunitinib.

To answer this question, the researchers calculated the amount of time that the participants lived with their PRCC without their tumors growing. This is called progression-free survival, also called PFS.

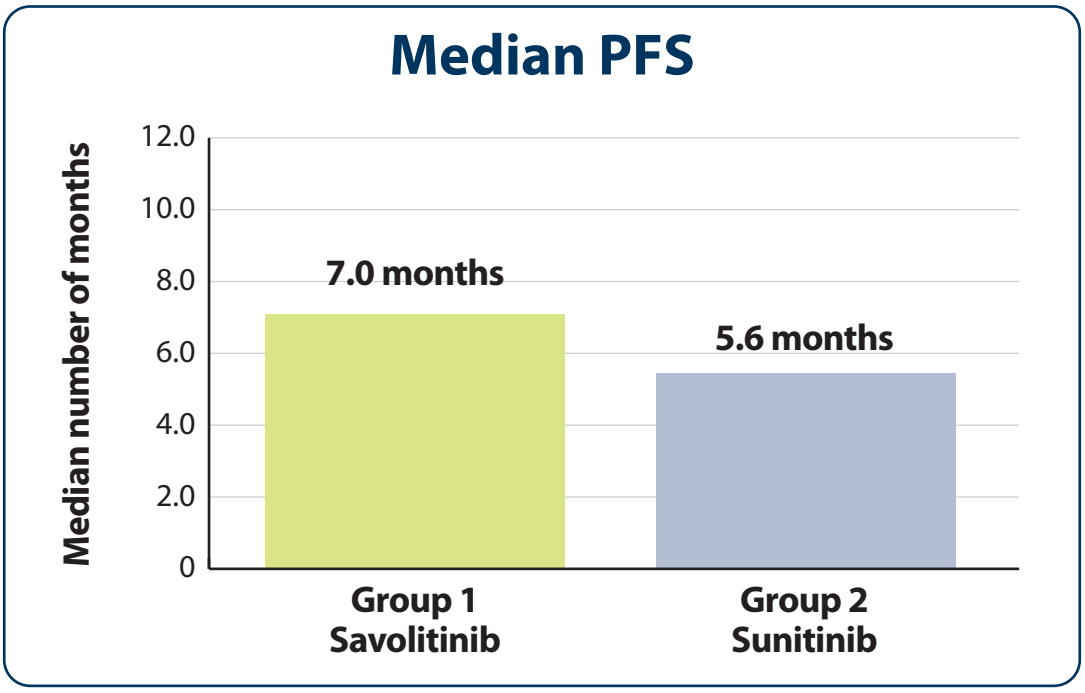
The doctors took pictures of the participants' tumors at different times throughout the study. They did this using CT or MRI scans to measure how long it took for tumors to grow a certain amount. This allowed the researchers to learn how each study treatment affected the size of the tumors during the study. To calculate the PFS, the researchers counted the number of months that the participants in each treatment group lived without their tumors growing. The researchers looked at these results using a median. A median is a kind of average. It is between the lowest and highest numbers.

They compared the results in the participants who took savolitinib and those who took sunitinib. The researchers found that the differences between the 2 treatment groups were too small to know if savolitinib slowed tumor growth compared to sunitinib.

The researchers found that the median PFS for each group was:

- 7.0 months in the participants who took savolitinib
- 5.6 months in the participants who took sunitinib

The chart below shows these results.



Did the participants' quality of life change after taking study treatment?

Overall, the researchers could not know if taking savolitinib changed the participants' quality of life compared to sunitinib.

To answer this question, the researchers used two surveys. The first was the Functional Assessment of Chronic Illness Therapy-Fatigue, also called FACIT-F. The other was the Functional Assessment of Cancer Therapy-Kidney Symptom Index-19, also called FKSI-19. These surveys asked the participants questions about their cancer symptoms and daily activities. The participants answered the surveys before they took study treatment, and throughout the study. The doctors gave the participants' symptoms scores based on their responses. In both surveys, a lower score meant a better quality of life.

The researchers found that both the participants who took savolitinib and those who took sunitinib had lower scores after taking study treatment than at the start of the study. But, there were not enough data points for the researchers to know if savolitinib changed the participants' quality of life compared to sunitinib.

FACIT-F scores

- The scores in the participants who took savolitinib were an average of 24.2 points lower at the end of the study.
- The scores in the participants who took sunitinib were an average of 23.3 points lower at the end of the study.

FKSI-19 scores

- The scores in the participants who took savolitinib were an average of 3.8 points lower at the end of the study.
- The scores in the participants who took sunitinib were an average of 8.0 points lower at the end of the study.

What medical problems did participants have during the study?

This section is a summary of the medical problems the participants had during the study that the doctors thought might be related to the study treatment.

These medical problems are called “adverse reactions”. An adverse reaction is considered “serious” when it is life-threatening, causes lasting problems, or requires hospital care.

These adverse reactions may or may not be caused by the study treatments. A lot of research is needed to know whether a treatment causes an adverse reaction.

The websites listed at the end of this summary may have other information about adverse reactions or other medical problems that happened during this study.

How many participants had serious adverse reactions?

There were 13.3% of participants who had serious adverse reactions during the study. This was 8 out of 60 participants.

There was 1 participant who died of a serious adverse reaction during the study. This participant took sunitinib and had a low level of blood cells that help clotting, called platelets.

The table below shows the serious adverse reactions that happened during the study. Some participants had more than one serious adverse reaction.

Serious adverse reactions during the study		
Serious adverse reaction	**Group 1 Savolitinib (Out of 33 participants)**	**Group 2 Sunitinib (Out of 27 participants)**
Lung infection	3.0% (1)	0.0% (0)
Allergic reaction to a drug	3.0% (1)	0.0% (0)
Blood clot in a vein	3.0% (1)	0.0% (0)
Build-up of fluid in the stomach area	3.0% (1)	0.0% (0)
Swelling in the legs and arms	3.0% (1)	0.0% (0)
A high amount of a liver enzyme (ALT)	3.0% (1)	0.0% (0)
A high amount of a liver enzyme (AST)	3.0% (1)	0.0% (0)
Low level of blood cells that help clotting (platelets)	0.0% (0)	3.7% (1)
Fast and abnormal heartbeat	0.0% (0)	3.7% (1)
Large increase in blood pressure without organ damage	0.0% (0)	3.7% (1)
PRCC got worse	0.0% (0)	3.7% (1)

How many participants had adverse reactions?

- 78.3% of participants had adverse reactions during the study. This was 47 out of 60 participants.
- 66.7% of participants had adverse reactions after taking savolitinib during the study. This was 22 out of 33 participants.
- 92.6% of participants had adverse reactions after taking sunitinib during the study. This was 25 out of 27 participants.

There were 15.2% of participants who stopped taking savolitinib because of adverse events they had during the study. This was 5 out of 33 participants.

There were 14.8% of participants who stopped taking sunitinib because of adverse events they had during the study. This was 4 out of 27 participants.

What adverse reactions did the participants have?

The most common adverse reaction was swelling in the arms and legs.

The table below shows the most common adverse reactions that happened in more than 4 participants during the study. There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions during the study

Adverse reaction	Group 1 Savolitinib (Out of 33 participants)	Group 2 Sunitinib (Out of 27 participants)
Swelling in the legs and arms	27.3% (9)	11.1% (3)
Feeling sick	6.1% (2)	25.9% (7)
Anemia (decrease in the number of red blood cells in the blood)	3.0% (1)	25.9% (7)
Not feeling as hungry as normal	3.0% (1)	25.9% (7)
Redness, swelling and pain on the hands and feet, also called Palmar-plantar erythrodysaesthesia syndrome	0.0% (0)	25.9% (7)
A high amount of a liver enzyme (AST)	15.2% (5)	7.4% (2)
High blood pressure	0.0% (0)	22.2% (6)
Diarrhea	0.0% (0)	22.2% (6)
A high amount of a liver enzyme (ALT)	15.2% (5)	3.7% (1)
Low numbers of white blood cells that fight infection	0.0% (0)	18.5% (5)
Vomiting	3.0% (1)	14.8% (4)
Feeling tired	3.0% (1)	14.8% (4)

How has this study helped patients and researchers?

This study helped researchers learn more about how savolitinib works compared to sunitinib in participants with advanced PRCC caused by changes in the MET gene.

Researchers look at the results of many studies to decide which treatments work best and are safest. This summary shows only the main results from this one study. Other studies may provide new information or different results.

Further clinical studies with savolitinib are planned.

Where can I learn more about this study?

You can find more information about this study on the websites listed below. If a full report of the study results is available, it can also be found here.

- www.clinicaltrials.gov. Once you are on the website, type **"NCT03091192"** into the search box, and click **"Search"**.
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2016-004108-73"** in the search box, and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D5082C00003"** into the search box, and click **"Find a Study"**.

Full Trial Title: A Phase III, Open Label, Randomised, Controlled, Multi-Centre Study to Assess the Efficacy and Safety of Savolitinib versus Sunitinib in Patients with MET-Driven, Unresectable and Locally Advanced, or Metastatic Papillary Renal Cell Carcinoma (PRCC)

National Clinical Trials Number: NCT03091192

AstraZeneca Protocol Number: D5082C00003

EudraCT Number: 2016-004108-73

AstraZeneca, sponsored this study and has its headquarters in Cambridge, UK.

The phone number for the AstraZeneca Information Center is +1-877-240-9479.

Thank you!

Clinical study participants belong to a large community of people who take part in clinical research around the world. They help researchers answer important health questions and find medical treatments for patients.

CISCRP

The Center for Information & Study on Clinical Research Participation (CISCRP) is a non-profit organization focused on educating and informing the public about clinical research participation. CISCRP is not involved in recruiting participants for clinical studies, nor is it involved in conducting clinical studies.

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