NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the effectiveness and safety of pazopanib and how it affects the quality of life in people with advanced and/or metastatic renal cell carcinoma after treatment with an immune checkpoint inhibitor.

Protocol number: CPZP034A2410

Thank You!

Novartis sponsored this trial and believes it is important to share what was learned from the results of this trial with the participants and the public.

Thanks to the participants for taking part in this trial for the drug pazopanib. They helped researchers learn more about how pazopanib works in people with advanced and/or metastatic renal cell carcinoma (RCC)

If you have any questions about the trial results, please talk to the doctor or staff at your trial site. The summary shows the results of a single clinical trial. Other clinical trials may have different findings.

Why was the research needed?

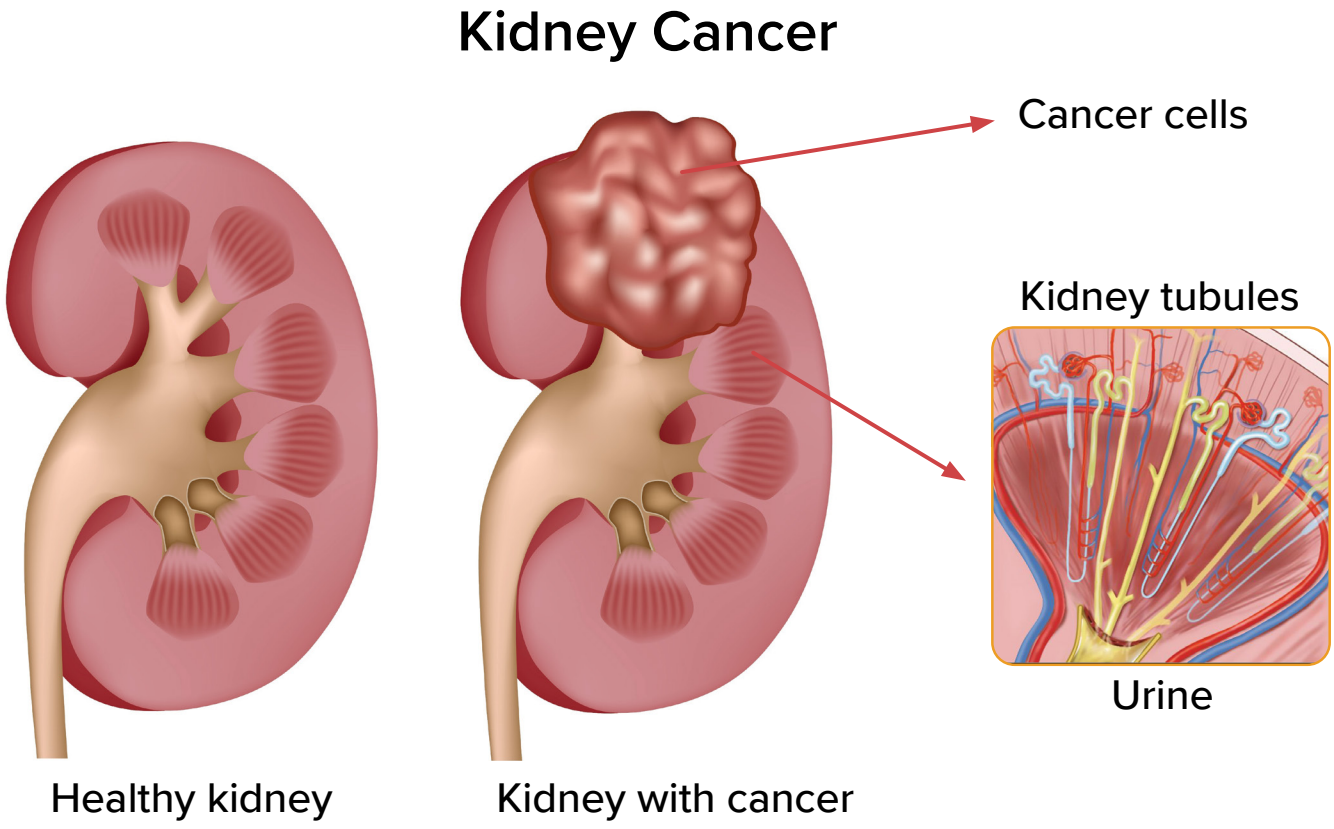
Researchers were looking for a better way to treat renal cell carcinoma (RCC). RCC is a type of cancer that begins in the tubules of the kidney. Tubules are tiny tubes that help filter toxic substances out of blood in order to make urine. When RCC spreads to other parts of the body, it is called metastatic RCC. RCC is the most common type of kidney cancer in adults.

One way to treat different types of cancer is by using Vascular Endothelial Growth Factor (VEGF) type of drugs such as pazopanib that target specific types of cancer cells. Pazopanib is approved in most countries for the treatment of advanced RCC and other types of cancer. These VEGF type of drugs slow down the growth of cancer cells by stopping the formation of the blood vessels that bring oxygen and food to these cells.

Another way to help fight off cancer is to boost the immune system. One group of drugs that can do this are called immune checkpoint inhibitors, which block a group of proteins called checkpoints. Checkpoints are proteins made by a person's immune system as well as some cancer cells to help prevent the immune system from killing cancer cells. Checkpoint inhibitors work by helping the immune system kill cancer cells easier.

These two groups of drugs have been used to treat RCC, but current research has shown that the effect may not last long and the cancer may eventually return.

The main purpose of this trial was to learn about the effectiveness and safety of pazopanib when given after previous treatment with immune checkpoint inhibitors in people with advanced and/or metastatic RCC.



Trial purpose

In this trial, researchers wanted to check if pazopanib works and is safe in patients with advanced and/or metastatic RCC who had previously been treated with checkpoint inhibitors but had never taken pazopanib before.

The main question the researchers wanted to answer in this trial was:

1. Did pazopanib increase the length of time participants lived with cancer, without their cancer getting worse (known as progression-free survival or PFS)?

Progression- free survival (PFS) is the length of time during and after the treatment of cancer that a patient lives with cancer without the disease getting worse. Progression-free survival is a good indicator of how well a particular cancer treatment works.

Second-line treatment is prescribed by doctors when the first treatment given to a patient with cancer does not work or has side effects that the patient cannot tolerate. If the second-line treatment doesn't work either or causes side effects that cannot be tolerated, then a third-line treatment is prescribed.

The other questions the researchers wanted to answer in this trial were:

1. What is the proportion (percentage) of participants whose cancer improves completely or partially or does not get worse after receiving pazopanib (also known as the clinical benefit rate of a drug)?
2. How long do the participants live after receiving pazopanib (also known as overall survival)?

How long was this trial?

This trial started in November 2017 and ended in August 2021. The entire duration, from enrolling the first participant to the last participant completing the trial was around four years. Individuals were in this trial until two years after the last participant was enrolled, or their disease progressed (got worse), or they could not be treated for any other reason, or died.

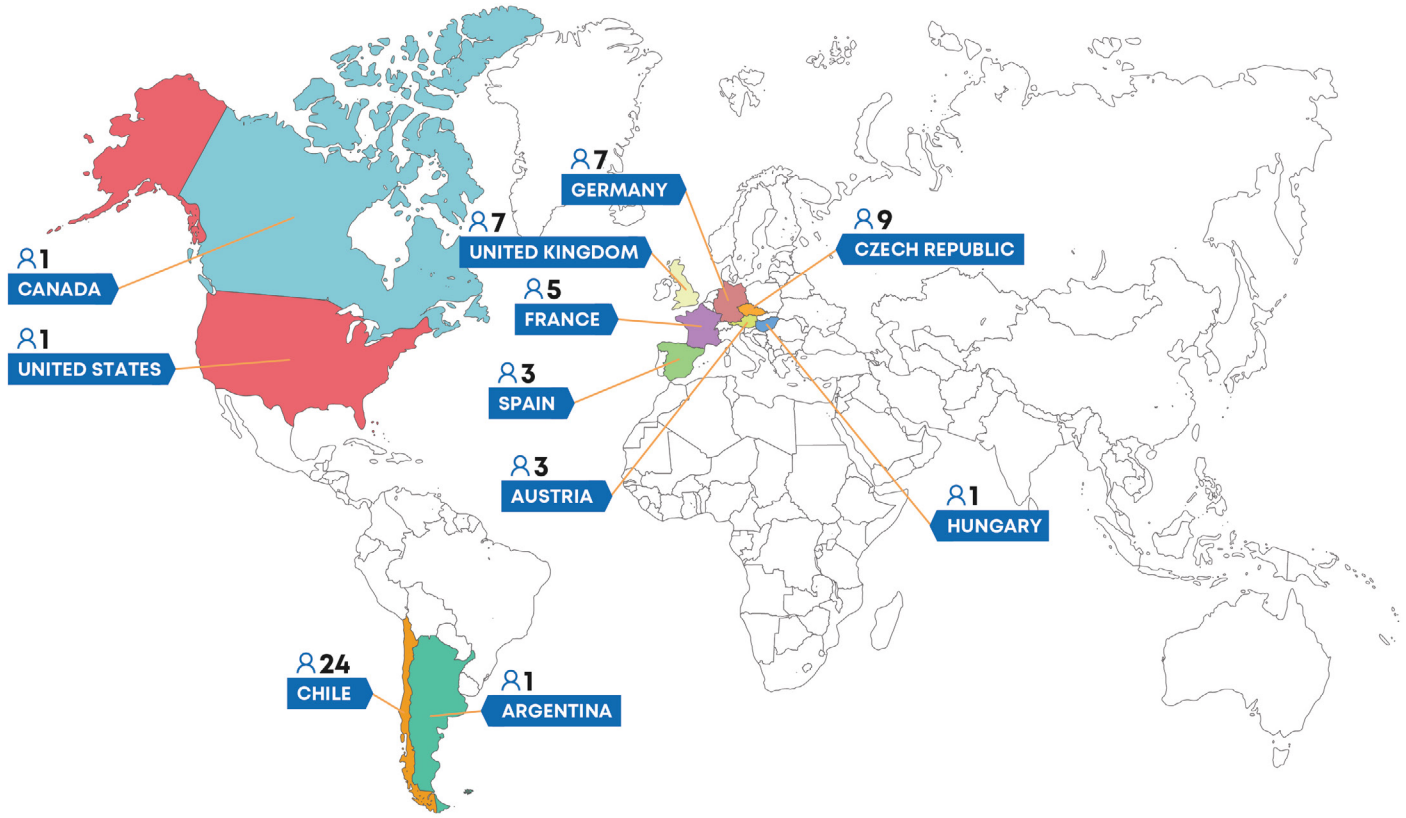
When the trial ended, researchers created a report of the trial results. This summary is based on that report.

Who was in this trial?

The participants could take part in this trial if they:

- were 18 years or older and had advanced or metastatic RCC (when RCC has spread to other parts of the body);
- had received a checkpoint inhibitor drug alone or in combination with another cancer-specific drug (as first or second-line treatment) four weeks or longer before starting the trial
- had the ability to tolerate the trial treatment;
- had normal levels of potassium, sodium, calcium, and magnesium;
- had not taken pazopanib previously.

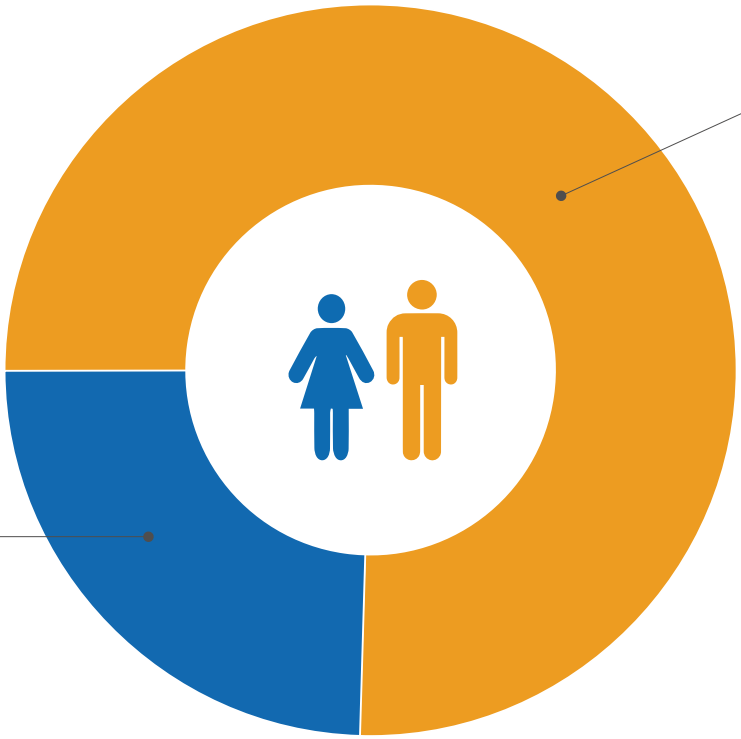
A total of **62 participants from 11 countries** participated in this trial.



The average age of participants in this trial was 63 years. The age of participants ranged from 39 to 84 years.

A total of 47 out of 62 (75.8%) trial participants received pazopanib as a second-line treatment, and 15 trial participants (24.2%) received the treatment as a third-line treatment.

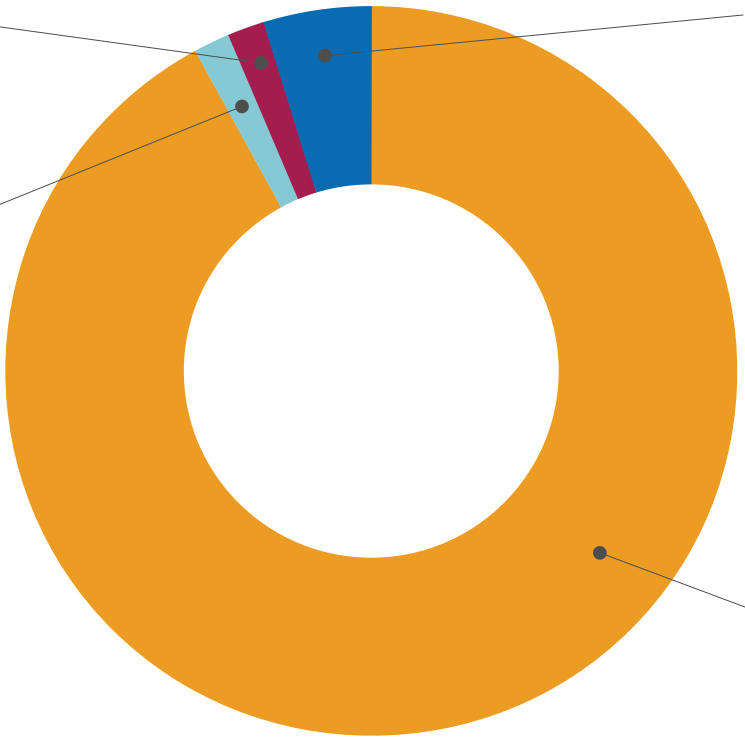
Participants' Gender



75.8%
OF PARTICIPANTS WERE MALE
(47 out of 62)

24.2%
OF PARTICIPANTS WERE FEMALE
(15 out of 62)

Participants' Race



1.6%
OTHER
(1 out of 62)

1.6%
ASIAN
(1 out of 62)

4.8%
UNKNOWN
(3 out of 62)

92%
WHITE
(57 out of 62)

What treatments did the participants take?

Trial drug:

The drug given in this trial was:

- Pazopanib given in a tablet form to be taken by mouth on an empty stomach, at the approved dose

Drug	*Pronounced as*
Pazopanib	paz-OH-pə-nib

What happened during this trial?

This was an open-label trial which means that the participants, trial doctors, and trial staff knew what treatment participants were receiving. All participants in this trial received the same treatment.

SCREENING

The doctors checked participants to make sure they could be in this clinical trial.

TREATMENT (Open-label)

Until 2 years

800 mg pazopanib once daily by mouth

FOLLOW-UP

Safety

From the end of treatment up to 1 month

Efficacy

From the end of treatment until worsening of cancer or until 1 year after the last participants was enrolled, every 2 months

Survival

From the end of treatment until 2 years after the last participants was enrolled, every 3 months

What were the main results of this trial?

Did pazopanib increase the length of time participants lived with cancer, without their cancer getting worse (known as progression-free survival or PFS)?

The results below are reported by median, which is the middle number between the highest and lowest numbers that the researchers observed.

Overall, at around 38 months after receiving pazopanib, the median length of time that participants lived after receiving treatment without their cancer getting worse was 6.8 months.

Looking at the median results, researchers found that the participants who took pazopanib as a second line treatment lived a median of 7.5 months without their cancer getting worse; and the participants who took pazopanib as a third line treatment lived a median of 4.6 months.

Overall, the proportion (percentage) of participants who lived with cancer, without their cancer getting worse (PFS) after 1 year was 31.2%. Researchers found that 36.4% of participants who took pazopanib as a second line treatment showed no worsening of cancer at 1 year and 14.3% of those who took pazopanib as a third line treatment showed no worsening of cancer at 1 year.

	Pazopanib Second-line Treatment (47 participants)	Pazopanib Third-line Treatment (15 participants)	All Participants (62 participants)
Median PFS	7.5 months	4.6 months	6.8 months
Participants who experienced progression or died	38 out of 47 (80.9%)	13 out of 15 (86.7%)	51 out of 62 (82.3%)
Participants who experienced cancer progression	32 out of 47 (68.1%)	11 out of 15 (73.3%)	43 out of 62 (69.4%)
Likelihood of PFS at 1 year	36.4%	14.3%	31.2%

What were the other results of this trial?

What was the proportion (percentage) of participants whose cancer improved completely or partially or did not get worse after receiving pazopanib (clinical benefit rate)?

A total of 53% of the patients who took pazopanib as a second-line treatment and 40% of those who took pazopanib as a third-line treatment, experienced clinical benefits.

How long did the participants live after receiving pazopanib (overall survival)?

Overall survival was 28 months for the patients who took pazopanib as a second-line treatment, and 20 months for those who took pazopanib as a third-line treatment.

What medical problems did the participants have during the trial?

Medical problems that happen in clinical trials are called "adverse events".

A lot of research is needed to know whether a drug causes an adverse event. During a trial, all adverse events are recorded, whether or not they are thought to be caused by the trial drug. When new drugs are being studied, researchers keep track of all adverse events participants have.

An adverse event is an unwanted sign, symptom, or disease that participants have during a trial.

An adverse event is considered "serious" when it is life threatening, causes lasting problems, or the participant needs hospital care. These problems may or may not be caused by the trial drug.

This section is a summary of the adverse events that happened during this trial. The websites listed at the end of this summary may have more information about all the adverse events that happened in this trial.

How many participants had adverse events?

The adverse events that happened during the trial are listed in the table below. In this trial, all 62 participants (100%) who received pazopanib reported at least 1 adverse event.

Number of Participants (%) with Adverse Events

	Number of Participants (out of 62)
At least 1 adverse event	62 (100%)
At least 1 serious adverse event	30 (48.4%)
Stopped drug due to adverse event	19 (30.6%)
Died	6 (9.7%)

How many patients died?

A total of 6 participants died while receiving pazopanib. Of those, a total of 5 participants died due to RCC while on study treatment and one participant died due to pulmonary sepsis (severe lung infection), which the trial doctors assessed as not caused by the trial drug.

How many participants stopped trial drug due to adverse events?

During the trial, 19 out of 62 (30.6%) participants stopped the treatment due to adverse events.

The most common adverse events that caused participants to stop pazopanib were high blood levels of a liver enzyme (alanine aminotransferase) in 6.5% of participants, liver damage (hepatotoxicity) in 4.8% of participants, and high blood levels of other liver enzymes (transaminases) in 3.2% of the participants.

What were the most common serious adverse events?

The most common serious adverse events that happened in at least 2 out of 62 participants (3.2%) are shown below:

Number of Participants (%) With Most Common Serious Adverse Events

	Number of participants (out of 62)
Alanine aminotransferase increase (higher blood levels of a liver enzyme due to liver damage)	5 (8.1%)
Hepatotoxicity (liver damage)	3 (4.8%)
Acute (short-term) **kidney injury**	2 (3.2%)
Back pain	2 (3.2%)
Hemoptysis (coughing blood)	2 (3.2%)
Pyrexia (fever)	2 (3.2%)
Transaminases increase (high blood levels of a liver enzyme due to liver damage)	2 (3.2%)
Urinary tract infection (bladder infection)	2 (3.2%)

What were the most common non-serious adverse events?

The most common non-serious adverse events that happened in at least 9 out of 62 participants (14.5 %) in any group are presented below.

Number of Participants (%) With Most Common Non-Serious Adverse Events

	Number of participants (out of 62)
Diarrhea	30 (48.4%)
Fatigue (excessive tiredness)	23 (37.1%)
Decreased appetite	17 (27.4%)
Hypertension (high blood pressure)	16 (25.8%)
Nausea	16 (25.8%)
Alanine aminotransferase increase (high blood levels of a liver enzyme due to liver damage)	12 (19.4%)
Dysgeusia (taste disturbance)	10 (16.1%)
Weight decreased	10 (16.1%)
Vomiting	9 (14.5%)
Aspartate aminotransferase increase (high blood levels of a liver enzyme due to liver damage)	9 (14.5%)

How was this trial useful?

This trial helped researchers learn about the effectiveness and safety of pazopanib in people with advanced and/or metastatic RCC, after treatment with checkpoint inhibitors.

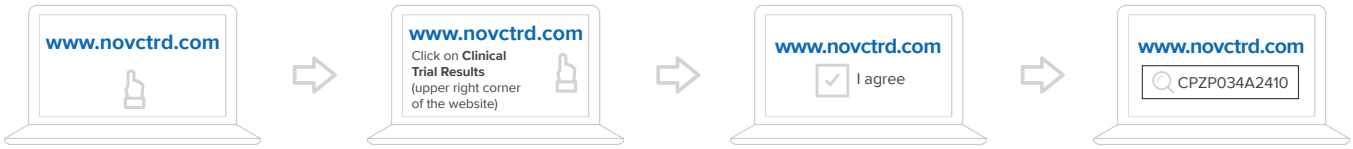
This shows that using pazopanib as a second-line treatment after previous treatment with checkpoint inhibitors may potentially be important for the successful management of cancer in people with advanced and/or metastatic RCC.

The safety and tolerability of pazopanib were consistent with what is known about this drug and acceptable for patients with RCC.

Where can I learn more about this trial?

More information about the results and adverse events in this trial can be found in the scientific summary of the results available on the Novartis Clinical Trial Results website (www.novctrd.com).

Please follow the below steps:



You can find more information about this trial on the following websites:

- www.clinicaltrials.gov Use the NCT identifier NCT03200717 in the search field.
- www.clinicaltrialsregister.eu/ctr-search Use the EudraCT identifier 2017-000708-10 in the search field.

Full clinical trial title: A prospective international multicenter Phase II study to evaluate the efficacy, safety, and quality of life of oral daily pazopanib in patients with advanced and/or metastatic renal cell carcinoma after previous therapy with checkpoint inhibitor treatment.

Thank You!

Thank you for taking part in this trial. As a clinical trial participant, you belong to a large community of people around the world. You helped researchers answer important health questions and test new medical treatments.

Novartis is a global healthcare company based in Switzerland that provides solutions to address the evolving needs of patients worldwide.
1-888-669-6682 (US); +41-61-324-1111 (EU);

www.novartisclinicaltrials.com

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