Clinical Trial Results – Layperson Summary

A study to look at how safe different doses of the study medicine (MOXR0916) were for patients with solid tumor cancer that had spread and did not respond to previous treatment(s), and how this medicine was processed by the body

See the end of the summary for the full title of the study.

About this summary

This is a summary of the results of a clinical trial; we will refer to the clinical trial as a "study" in this document.

This summary is written for:

- Members of the public.
- Patients who took part in the study, called "participants".

This summary is based on information known at the time of writing.

The study started in July 2014 and finished in August 2019. This summary was written after the study had ended.

No single study can tell us everything about the risks and benefits of a medicine. Many patients volunteer in several studies to help us find out everything we need to know.

The results from this one study may be different from other studies with the same medicine.

- You should not make decisions based on this one summary.
- Always speak to your doctor before making any decisions about your treatment.

Contents of the summary

Thank you to the people who took part in this study

The people who took part have helped researchers to gather important information about the study medicine and any signs of whether it could be effective on cancers in different parts of the body.

Key information about this study

This study was done to find out what the safe dose was for a new medicine for cancer.

- In this study, patients got a new medicine called MOXR0916. Different patients got different amounts of the medicine.
- Researchers wanted to know what dose or how much of the medicine was safe for patients to get into their bodies through IV.
- Researchers also wanted to know what happened to the medicine in the body and whether the medicine had any effect on the cancer.
- This study included 174 patients in 6 countries.
- The main discovery was that this medicine (MOXR0916) was safe for patients at all the doses tested.
- Around 3% of patients who got MOXR0916 had serious side effects.
- The researchers looked at results from all the doses studied. They picked a single dose that they thought would be useful in future studies.

1. General information about this study

Why was this study done?

This study was done to test the safety of an experimental medicine in patients with solid tumor cancer that had grown or spread and did not respond to previous treatment(s).

Researchers wanted to find out what dose of the study medicine, MOXR0916, was safe to give to cancer patients and what effects, good and/or bad, it had on patients and on their cancers.

This was the first time MOXR0916 was given to humans.

What was the study medicine?

MOXR0916 is a new medicine designed to work on the immune system, and this type of medicine is known as an **immunotherapy**. There are different kinds of immunotherapies and MOXR0916 is an **antibody immunotherapy**.

- Antibodies are proteins that only bind to one target. MOXR0916 was designed to only bind to OX40.
- By binding to OX40 present on T cells in the human body, MOXR0916 could cause T cells to divide and increase the number of T cells in the body. MOXR0916 could also help the T cells to survive longer.
- More T cells could mean a stronger immune system to fight cancer cells.

What did researchers want to find out?

- Researchers did this study to compare different doses of the new medicine that was given to patients once every 3 weeks by intravenous (IV) infusion into their blood veins.

- Researchers wanted to find out how many people had side effects at each dose after getting the medicine during this study.

The main questions that researchers wanted to answer were:

1. What doses of MOXR0916 could be considered safe for patients?
2. What was the largest dose of MOXR0916 that could be tolerated?
3. Were there any side effects that limited how much medicine a patient should get?
4. Based on the results of this study, what dose of MOXR0916 do researchers recommend should be given to patients in future studies?

Other questions that researchers wanted to answer included:

5. What happened to MOXR0916 in the body when patients took this medicine?
6. Does MOXR0916 cause any reactions in the immune system?
7. Does MOXR0916 have any effect on cancer?

What kind of study was this?

This was a "**Phase 1**" study, which means that this was one of the first studies for MOXR0916. If fact, this was the first time that this medicine was given to patients.

This study was considered "**open label**" because doctors and patients knew what medicine the patients were getting, and which dose they were getting.

One part of the study was called "**dose escalation**", which means that every new group of patients got higher doses of the medicine. However, if a certain number of patients got certain side effects after taking one dose of the medicine, then the next group could not get a higher dose of the medicine.

Researchers studied results for the different doses of MOXR0916 with small groups of patients. Following this, patients were enrolled in "**dose expansion**" to study a single dose (300 mg) of MOXR0916 in larger groups of patients diagnosed with lung, breast, kidney, skin or bladder cancers. This allowed the researchers to study a particular dose of this medicine in a larger number of patients.

When and where did the study take place?

The study started in July 2014 and finished in August 2019. This summary was written after the study had ended.

The study took place at 4 centers in Australia, 3 centers in Belgium, 5 centers in Canada, 4 centers in Spain, 3 centers in South Korea, and 12 centers in the United States of America.

2. Who took part in this study?

There were **174 patients** who took part in this study. Among them, 172 patients provided results on the safety of the medicine, and 162 patients provided results on whether the medicine was effective for cancer patients.

- The youngest patient was 22 years old while the oldest patient was 88 years old. Half of the patients were under 59 years old (median age).
- The majority of the patients (75%) were white. Over half of the patients (59%) were men and less than half of the patients (41%) were women.
- Patients with several different kinds of cancers could take part in this study but only if doctors thought that there was no other medicine that could be useful.
- Some patients had "locally advanced" cancer that could not be treated completely by surgery or radiation. Others had "metastatic" cancer – which means that their cancer had spread to other parts of the body.

Patients could take part in this study if:

- They were at least or over 18 years old.
- They had locally advanced or metastatic incurable cancer, and no other effective medicine was available.
- They were healthy enough for the study, with functioning liver, kidney, and blood system.
- In addition, patients joining the dose expansion groups had additional rules for enrollment. Some of these groups only enrolled patients with certain types of cancer. Some of the groups only enrolled patients who agreed to provide biopsy samples at different times during the study.

Patient could not take part in the study if:

- They had received another type of cancer treatment within the last 3 weeks before the start of this study.
- They had certain diseases or infections present at the time of the study.
- They had experienced certain diseases or infections in the past.
- They had any major surgery within last 4 weeks.
- Mothers who were nursing or who were pregnant were not allowed to take part in the study.

3. What happened during the study?

Patients joined the study at different times starting in 2014.

- During the study, patients received MOXR0916 by IV once every 3 weeks.
- One dose at a time was studied in one group of patients before the next group of patients got the next higher dose.
- In "dose escalation", those patients who joined the study earlier got smaller doses of the medicine while patients who joined later received higher doses.
- In "dose expansion", some patients joined groups according to the type of cancer they had. Some patients agreed to provide biopsy samples.
- Patients were allowed to get off the study at any time if they chose to do so, or if their doctors thought that that was the right decision.
- Patients received follow-up phone calls after they stopped their treatment. This happened every 3 months.

Study drug dose

Of the 174 patients who enrolled in this study, 172 patients got MOXR0916 treatment. Most patients received more than one treatment, and up to 72 treatments per patient were given.

Patients in this study joined one of 10 dose groups (0.2 to 1200 mg) in the dose escalation part of the study. In the dose expansion part of the study, they received one of 7 doses (3.2 to 600 mg).

Here is a table for the number of patients in each dose group for the entire study:

MOXR0916 – dose of medicine	Number of patients who got this dose
0.2	3
0.8	3
3.2	6
12	11
40	7
80	12
160	11
300	109
600	6
1200	4
Total number of patients who got study medicine	**172**

Time on study

Most patients received treatment for 64 days (median) while others left early or stayed longer. The longest time for treatment was 1596 days (over 4 years).

What was done on the study

Patients were seen by their doctors on a regular basis. The doctors collected samples from patients for lab analyses and also did tests. Doctors also spoke with patients to find out how patients were reacting to the medicine. Doctors took note of any side effects due to MOXR0916. If the side effects were minor, doctors gave out treatments for the side

effects. Patients were taken off the study treatment if their doctors thought it was the right decision.

4. What were the results of the study?

Question 1: What doses of MOXR0916 could be considered safe for patients?

Researchers looked at 10 different doses of MOXR0916. This study showed that all doses were safe for patients and that the side effects could be managed by doctors.

Question 2: What was the largest dose of MOXR0916 that could be tolerated?

During dose escalation, the largest dose given to patients was 1200 mg, which was safe. Researchers did not go beyond this dose, so they did not find the dose that patients should not exceed.

Question 3: Were there any side effects that limited how much medicine a patient should get?

Researchers did not find any side effects that would limit giving MOXR0916 to patients at the doses tested.

Question 4: Based on the results of this study, what dose of MOXR0916 do researchers recommend should be given to patients in future studies?

Based on the results of this study, researchers decided on **a fixed dose of 300 mg given by IV once every 3 weeks**, for future studies.

Question 5: What happened to MOXR0916 in the body when patients took this medicine?

Patients received their treatment once every 3 weeks. At doses between 80 and 1200 mg given once every 3 weeks, researchers found that MOXR0916 fell to half its peak concentration in the body by 11-22 days after administration.

Question 6: Does MOXR0916 cause any reactions in the immune system?

Researchers found that 3% of patients had antibodies in their immune systems ("anti-drug antibodies" or ADAs) that reacted against MOXR0916 before receiving the first dose of the study medicine.

After receiving the study medicine, 19% of patients tested positive for ADAs. In some patients, the ADA was associated with a change in how quickly MOXR0916 was removed from the body.

The impact of these ADAs on the safety or anti-cancer effect of MOXR0916 was not studied.

Question 7: Does MOXR0916 have any effect on cancer?

Researchers looked to see if there was any effect of this medicine on cancer in patients on the study. They found that 57 patients (33%) had "**stable disease**" (no change), 104 patients (61%) had "**progressive disease**" (became worse over time), while 10 patients (6%) did not have results available. Two patients in this study had a "**partial response**" (cancer got smaller by a small amount) in response to MOXR0916 treatment.

5. What were the side effects?

Side effects (also known as "adverse reactions") are unwanted medical problems (such as a headache) that happen during the study.

- No one in this study had all of the side effects.
- Some patients had a few of the side effects.

Serious and common side effects are listed below:

Serious side effects

A side effect is considered "serious" if it is life-threatening, needs hospital care, or causes lasting problems.

During this study, 5 patients (3%) reported having a serious side effect thought to be related to the study medicine:

- Labored breathing (dyspnea exertional)
- Inflamed membrane surrounding the heart (pericarditis)
- Water on the lungs (pleural effusion)
- Inflammation of the liver (autoimmune hepatitis)
- Inflammation of the digestive tract (colitis)

Deaths

A total of 111 deaths were reported in this study. None of the deaths were caused by the study medicine.

Among the 111 deaths,

- 46 deaths were reported during 90 days after the last MOXR0916 treatment.
  None of these deaths were caused by the study medicine:
  42 deaths were due to the disease becoming worse (disease progression)
  2 deaths were due to bleeding in the belly
  1 death due to lung infection (pneumonia)
  1 death due to failure of the lungs (respiratory failure).
- 65 deaths occurred beyond 90 days after the last MOXR0916 treatment.

Most common side effects

During this study, around 57% of patients had a side effect that was not considered serious but was thought to be caused by the study medicine

Several side effects were reported, but this summary only lists the most common ones that happened to more than 5% of the patients.

Common side effects	What percentage of patients got this side effect
Feeling tired (fatigue)	17%
Diarrhea	8%
Muscle pain (myalgia)	7%
Feeling sick (nausea)	6%
Not hungry (decreased appetite)	6%
Allergic reaction to treatment (infusion-related reaction)	5%

Other side effects

You can find information about other side effects (not shown in the sections above) on the websites listed at the end of this summary – see section 8.

6. How has this study helped research?

The results presented here are from a single study of 174 patients with several different kinds of cancer. These results helped researchers learn more about MOXR0916:

- What dose of this medicine can be used safely in future studies.

No single study can tell us everything about the risks and benefits of a medicine. The results from this study may be different from other studies with the same medicine.

- This means that you should not make decisions based on this one summary.
- Always speak to your doctor before making any decisions about your treatment.

7. Are there plans for other studies?

Several studies with patients who have different kinds of cancers and who were given MOXR0916 were carried out. Clinical studies of MOXR0916 can be found at:

https://clinicaltrials.gov/ct2/results?cond=&term=MOXR0916&cntry=&state=&city=&dist=
https://www.clinicaltrialsregister.eu/ctr-search/search?query=moxr0916

8. Where can I find more information?

You can find more information about this study on the website listed below:

- https://clinicaltrials.gov/ct2/show/NCT02219724

Who can I contact if I have questions about this study?

If you have any further questions after reading this summary:

- Visit the ForPatients platform and fill out the contact form
  https://forpatients.roche.com/en/About.html
- Or, contact a representative at your local Roche office.

If you took part in this study and have any questions about the results:

- Speak with the study doctor or staff at the study hospital or clinic.

If you have questions about your own treatment:

- Speak to the doctor in charge of your treatment.

Who organized and paid for this study?

This study was organized and paid for by Genentech, Inc., South San Francisco, CA, USA. Genentech is part of F. Hoffmann-La Roche Ltd., with headquarters in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study is: “A phase 1, open label, dose-escalation study of the safety and pharmacokinetics of MOXR0916 administered intravenously as a single agent to patients with locally advanced or metastatic solid tumors”.

- The protocol number for this study is: GO29313.
- The ClinicalTrials.gov identifier for this study is: NCT02219724.