Summary of Clinical Trial Results

A study to look at how safe different doses of MOXR0916 were for patients with cancer – when combined with one or two other medicines

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 (called a "study" in this document).

This summary is written for:

- Members of the public
- Participants – these are patients who took part in this study

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

The study started in October 2015 and finished in November 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.

It takes lots of people in many studies to find out everything we need to know.

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.**

Contents of the summary

Thank you to the people who took part in this study

The patients who took part have helped researchers answer important questions about MOXR0916 and cancer.

Key information about this study

- This study was done to find out if MOXR0916 was safe in combination with one or two other medicines, for patients with cancer.
- In this study, patients were given MOXR0916 at different doses, with a fixed dose of atezolizumab. A few patients got MOXR0916 + atezolizumab + bevacizumab.
- This study included 298 patients in seven countries.
- The main finding was that MOXR0916 was safe for patients, when given in combination with atezolizumab.
- Around 3% of patients (9 out of 298) taking MOXR0916 had serious side effects, thought to be related to the study medicine.
- This summary was written after the study was completed.

1. General information about this study

Why was this study done?

There are several experimental medicines for cancer that work by getting the patient's own immune system to recognize and kill cancer cells. These types of medicines are called "**immunotherapies**".

Immunotherapies have shown some benefit in patients with cancer. But over time, the cancer gradually becomes resistant to the treatment, and stops responding.

Researchers believe that combining different types of immunotherapies may be better at battling cancers and overcoming resistance.

This study was done to find out if it was safe to combine an immunotherapy (MOXR0916) with another (atezolizumab), and in some cases a third anti-cancer medicine (bevacizumab).

What were the study medicines?

All patients were treated with MOXR0916 and atezolizumab. A few patients also received a third medicine (bevacizumab).

MOXR0916

- This medicine is known as an "antibody immunotherapy**"**.
- It is an experimental medicine.
- MOXR0916 binds to a protein called "OX40", present on T cells.
- This causes T cells to make more 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

Atezolizumab

- This medicine is known as an "antibody immunotherapy".
- It is approved for the treatment of certain types of cancers.
- Atezolizumab binds to a protein called "PD-L1".
- PD-L1 is present on several human tumors, and causes the immune system to become tolerant of the cancer.
- By binding and inactivating PD-L1, atezolizumab improves the immune system's ability to fight cancer.

Bevacizumab

- This medicine is known as an "anti-angiogenic antibody" – a medicine that stops the growth of blood vessels.
- It is approved for use in several diseases.
- Bevacizumab binds to a protein that circulates in the body, called "VEGF".
- VEGF is a protein that binds to cells and causes the growth of blood vessels.
- By binding to and reducing VEGF in the body, bevacizumab lowers the ability of tumors to grow blood vessels.

What did researchers want to find out?

Researchers wanted to if it was safe to combine MOXR0916 with one or two of the other medicines in this study.

The main question that researchers wanted to answer was:

1. Is MOXR0916 in combination with atezolizumab – safe for patients - when given with and without bevacizumab?

Another question that researchers wanted to answer was:

2. Did the treatments have any effect on the tumors?

What kind of study was this?

This was a "**Phase 1b**" study, which means that this was one of the early studies for MOXR0916. In addition, different doses of this medicine were investigated in combination with one or two other medicines.

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, then the next group could not get a higher dose of the medicine.

Following dose escalation, patients were enrolled in "**dose expansion**" to study more patients at a few select doses of MOXR0916.

This allowed researchers to study a particular dose of MOXR0916 in combination with atezolizumab with or without bevacizumab in different type of cancers in more detail and in a larger number of patients.

When and where did the study take place?

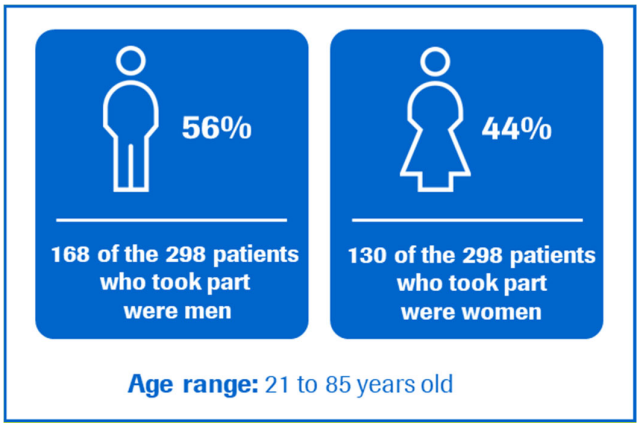
The study started in October 2015 and finished in November 2019. This summary was written after the study had ended.

The study took place at 25 study centers in 7 countries:

- Australia (3 study centers)
- Belgium (3 study centers)
- Canada (3 study centers)
- Spain (4 study centers)
- France (1 study center)
- Korea (3 study centers)
- USA (8 study centers)

2. Who took part in this study?

A total of 298 patients took part in this study. There were 35 patients who joined dose escalation. There were 263 patients in dose expansion who had lung, breast, bladder, kidney, or skin cancer.



Patients could take part in the study if:

- They were at least 18 years of age.
- Doctors thought the patients had a life expectancy of at least 12 weeks.
- They had cancer that was advanced, came back (recurrent), or had spread (metastasized), and that could not be cured.
- In some groups, patients needed to have tumors that could be sampled with a needle biopsy.
- In some groups, patients could only join if they had certain types of cancers.
- In some groups, patients could only join if they had been previously treated with a certain cancer therapy (PD-L1/PD-1 inhibitor).

Patients could not take part in this study if:

- They had heart disease, liver disease, lung disease, recent surgery, and certain other diseases.
- They had recently received certain medicines.
- They had undergone bone marrow or organ transplant.
- They were allergic to certain medicines.

3. What happened during the study?

During the dose-escalation stage of the study, patients joined a low dose group if they joined the study early. Those who joined the study late got the higher dose groups.

In dose-expansion, patients joined groups according to the type of tumors they had, and whether doctors could take samples of the tumor tissue (do needle biopsies).

Treatments:

- Patients got their treatment through an IV (intravenously) once every 3 weeks.
- The treatment included different doses of MOXR0916 for different groups of patients, and a fixed dose of atezolizumab (1200 mg).
- Patients in the dose expansion groups got a fixed dose of MOXR0916 (300 mg) and a fixed dose of atezolizumab (1200 mg).
- Some patients got a third medicine in their IV – bevacizumab – which was given according to body weight (15 mg/kg).

Here are the treatments that patients got:

Treatment	Number of patients
0.8 mg MOXR0916 + atezolizumab	3
3.2 mg MOXR0916 + atezolizumab	4
12 mg MOXR0916 + atezolizumab	6
40 mg MOXR0916 + atezolizumab	8
130 mg MOXR0916 + atezolizumab	10
300 mg MOXR0916 + atezolizumab	247
600 mg MOXR0916 + atezolizumab	4
1200 mg MOXR0916 + atezolizumab	4
300 mg MOXR0916 + atezolizumab + bevacizumab	9
600 mg MOXR0916 + atezolizumab + bevacizumab	3

What was done on the study

Patients were seen by their doctors on a regular basis. Doctors collected patient samples for lab analyses and also did tests. Doctors found out how patients were reacting to the treatment. They noted and treated any side effects that the patients got.

How much medicine did patients get

Patients and their doctors could decide to stop their treatments at any time. Half of the patients received up to 4 cycles of MOXR0916 (median number of cycles). A cycle of treatment meant one treatment given every 3 weeks. Some patients received up to 64 cycles (range 1 to 64 treatments).

What happened to patients on the study

All 298 patients (100%) who received treatment stopped the study.

- 161patients (54%) died while on the study.
- 38 patients (13%) withdrew from the study.
- 13 patients (4%) stopped because the sponsor stopped the study.
- 6 patients (2%) were lost to follow-up.
- 91 patients (31%) had other reasons than those listed above.

4. What were the results of the study?

This section only shows the key results from this study. You can find information about all other results on the websites at the end of this summary (see section 8).

Question 1: Is MOXR0916 in combination with atezolizumab – safe for patients - when given with and without bevacizumab?

Researchers found MOXR0916 in combination with atezolizumab, with or without bevacizumab, to be safe and acceptable for patients with cancer. Side effects are listed in the next section.

Question 2: Did the treatments have any effect on the tumors?

Twelve patients (4%) responded favorably to study treatment (cancer got smaller or could no longer can be detected). This included one patient with breast cancer who showed a complete response, and 11 patients with lung, kidney, bladder, breast, ovarian and skin cancers who showed partial response (cancer got smaller).

In 102 patients (34%), the disease remained stable during the study. For 164 patients (55%), the disease became worse (disease progression).

For 20 patients (7%), the treatment effect (outcome) was missing or could not be evaluated.

5. What were the side effects?

Side effects are medical problems (such as feeling dizzy) that happen during the study.

- They are described in this summary because the study doctor believes the side effects were related to the treatments in the study.
- Not all of the patients in this study had all of the side effects.
- Side effects may be mild to very serious, and can be different from person to person.
- It is important to be aware that the side effects reported here are from this single study. Therefore, the side effects shown here may be different from those seen in other studies, or those that appear on the medicine leaflets.
- Serious and common side effects are listed in the following sections.

Serious side effects

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

There were a total of 11 serious side effects thought to be related to MOXR0916, which occurred in 9 patients:

Serious side effects related to MOXR0916	Number of patients who experienced this
Reaction to getting treatment through an IV (infusion-related reaction)	3 patients
Water on the lungs (pleural effusion)	2 patients
Inflammation of lung tissue (pneumonitis)	1 patient
Overactive thyroid gland (hyperthyroidism)	1 patient
Reduced blood flow to part of the large intestine (colitis ischemic)	1 patient
Weakness of the heart - slowed blood pumping (cardiac failure)	1 patient

Patient deaths

Overall, 161 patients (54%) died during the study. None of the patient deaths were thought to be caused by MOXR0916.

Among the 161 deaths,

- 145 deaths were due to disease progression
- 8 deaths were due to side effects such as aspiration (breathing in of solids/liquids into the lungs), heart attack, bleeding in the brain, infection of chronic lung disease, blood clot in the lung blood vessels, failure of the lungs, sepsis and septic shock (severe infection in the bloodstream due to bacteria/viruses).
- 8 deaths were due to unknown cause.

Stopping treatment because of side effects

During the study, 18 patients (6%) decided to stop their treatment because of side effects.

Most common side effects

During this study, 134 patients (45%) reported a side effect that was not considered serious, but thought to be caused by any of the 3 study medicines.

Some people had more than one side effect – this means that they are included in more than one row in the table below. Only the most common events – those seen in 6 or more patients – are listed here.

Commons side effects that were not serious	Number of patients who experienced this
Feeling tired (fatigue)	39 patients (13%)
Allergic reaction to IV treatment (infusion-related reaction)	21 patients (7%)
Diarrhea	20 patients (7%)
Feeling sick to stomach (nausea)	18 patients (6%)
Not hungry (decreased appetite)	15 patients (5%)
Rash	12 patients (4%)
Muscle ache (myalgia)	10 patients (3%)
Fever (pyrexia)	9 patients (3%)
Headache	9 patients (3%)
Itchy skin (pruritus)	8 patients (3%)
Underactive thyroid gland (hypothyroidism)	8 patients (3%)
Dry skin	7 patients (2%)
Feeling weak (asthenia)	6 patients (2%)
High blood pressure (hypertension)	6 patients (2%)
Joint pain (arthralgia)	6 patients (2%)
Vomiting	6 patients (2%)

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 information presented here is from a single study of 298 patients with several kinds of cancers. These results helped researchers learn more about cancer and medicines known as immunotherapies.

Researchers learned that the immunotherapies in this study can be safely combined for treating patients who have cancer.

Based on the results of this and other studies, researchers will not study MOXR0916 in future studies.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. 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?

MOXR0916 will not be studied further. Studies that have occurred can be found at:

https://www.clinicaltrialsregister.eu/ctr-search/search?query=moxr0916

https://clinicaltrials.gov/ct2/results?cond=&term=MOXR0916&cntry=&state=&city=&dist=

8. Where can I find more information?

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

https://clinicaltrials.gov/ct2/show/results/NCT02410512

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
- 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 the study is:

A Phase 1b, Open-Label, Dose-Escalation Study of the Safety and Pharmacokinetics of MOXR0916 and Atezolizumab with Bevacizumab in Patients with Locally Advanced or Metastatic Solid Tumors.

- The protocol number for this study is **GO29674**.
- The ClinicalTrials.gov identifier for this study is **NCT02410512**.
- The EudraCT number for this study is **2015-000516-18**.