Clinical Trial Results – Layperson Summary

A study of a medicine (GDC-0919) combined with another medicine (atezolizumab) in patients with cancer that has grown or spread

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 2015 and finished in October 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.

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Thank you to the people who took part in this study

The patients who took part in this study have helped researchers to gather important information about the study medicines and any signs of added benefit from combining the two medicines for the treatment for 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 medicine (GDC-0919) when it was combined with another medicine (atezolizumab) for treating cancer.
- All patients got the same dose of atezolizumab.
- Different groups of patients got different doses of GDC-0919.
- This study included 158 cancer patients in four countries.
- Combination therapy with GDC-0919 and atezolizumab was thought to be generally safe.
- Around 75% of patients got common side effects and 10% got serious side effects. These common and serious side effects were thought to be caused by the study medicine.
- Taking two medicines together did not interfere with each other. Each medicine was absorbed rapidly and the amount absorbed was related to the dose of the medicine.
- Combining the two medicines did not improve the effectiveness of the medicines. Based on this, the study stopped enrolling new patients.

1. General information about this study

Why was this study done?

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

Researchers wanted to find out what dose of the study medicine (GDC-0919) was safe to combine with another medicine (atezolizumab).

GDC-0919 is a medicine that blocks a protein called "**IDO1**". Atezolizumab works by blocking a protein called "**PD-L1**". These proteins have an effect on the immune system of the patient.

One function of the immune system is to detect and eliminate cancer cells. However, both IDO1 and PD-L1 allow cancer cells to escape the immune system.

Researchers believe that combining GDC-0919 and atezolizumab may help boost the immune system of cancer patients, and stop or reverse the growth of tumors.

GDC-0919 has previously been investigated in patients as a "**single agent**", which means it was given alone without any other cancer treatments. Atezolizumab has been investigated as a single agent as well.

The combination of GDC-0919 and atezolizumab in this study is **experimental**; this combination is not approved by the United States Food and Drug Administration (FDA).

The **combination treatment** was given to cancer patients to find out what effects, good and/or bad, GDC-0919 and atezolizumab had on patients and on their cancers.

What was the study medicine?

GDC-0919 is a study medicine designed to work on the IDO1 protein in the immune system.

- IDO1 is expressed by several human tumors.
- The expression of IDO1 has an effect on the immune system: IDO1 makes the immune system tolerant of cancer cells.
- GDC-0919 is a "**small molecule**" medicine that stops the activity of IDO1 protein.
- GDC-0919 may be able to improve the immune system's ability to fight cancer.

Atezolizumab is a study medicine designed to work on the PD-L1 protein in the immune system.

- Atezolizumab is a type of medicine known as an "**antibody immunotherapy"**.
- Antibodies are proteins that only bind to one target.
- Atezolizumab was designed to only bind to PD-L1.
- PD-L1 is expressed by several human tumors.
- PD-L1 causes the immune system to become tolerant of the cancer.
- Atezolizumab can bind to and inactivate PD-L1.
- Atezolizumab may be able to improve the immune system's ability to fight cancer.
- Atezolizumab is approved to treat certain types of cancers.

What did researchers want to find out?

Combination therapy

Researchers wanted to find out if GDC-0919 could be safely combined with atezolizumab for treatment of cancer in patients.

The main question that researchers wanted to answer was:

1. Was it safe and could the side effects be tolerated when patients received treatment that combined GDC-0919 and atezolizumab?

Other questions that researchers wanted to answer included:

2. What was the largest dose of GDC-0919 that could be combined with a fixed dose of atezolizumab?
3. What happens to GDC-0919 and atezolizumab in the body when given as a combination treatment?
4. Does the combination treatment improve the outcome for patients when compared to studies where patients got these medicines as a single agent?

What kind of study was this?

This was a "**Phase 1b**" study, which means that this was one of the early studies for GDC-0919. In addition, different doses of this medicine were investigated in combination with another medicine.

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.

While all patients got the same dose of atezolizumab, researchers investigated different doses of GDC-0919 in small groups of patients. Following this, patients were enrolled in "**dose expansion**" to study two different doses of GDC-0919 given with the same dose of atezolizumab. This allowed the researchers to study a particular dose of GDC-0919 in combination with atezolizumab in a larger number of patients.

When and where did the study take place?

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

The study took place at 18 study centers in four countries including United States (10 centers), Korea (3 centers), Spain (3 centers), and France (2 centers).

2. Who took part in this study?

There were **158 patients** who took part in this study. Among them, one patient did not get any medicine; 5 patients did not get any GDC-0919 (but did receive atezolizumab); 3 patients did not get an atezolizumab (but did receive GDC-0919).

One hundred and fifty-seven patients who got at least one dose of either medicine provided results on the safety of the treatment. All 158 patients provided results on the outcome of their disease at the end of the study.

Patients:

- The youngest patient was 31 years old while the oldest patient was 80 years old. Half of the patients were under 60 years old (median age).
- The majority of the patients (70%) were white. Over half of the patients (58%) were women and less than half of the patients (42%) were men.
- 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 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 enrolled patients who had previously received a certain type of cancer treatment and had shown improvements for some time before the cancer came back (relapse).

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?

In this study, some patients joined the "dose escalation" groups while others joined the "dose expansion" groups.

Dose escalation groups

- Patients received a fixed dose of atezolizumab (1200 mg) by IV once every 3 weeks.
- They also took GDC-0919 pills by mouth, twice daily.
- Patients in different groups got different doses of GDC-0919.
- One dose of GDC-0919 at a time was studied in one group of patients before the next group got the next higher dose.
- Those patients who joined the study earlier got lower doses of GDC-0919 while patients who joined later received higher doses.

Patient group by medicine dose	Number of patients in this group
GDC-0919 (**50 mg**) + atezolizumab (1200 mg)	6
GDC-0919 (**100 mg**) + atezolizumab (1200 mg)	7
GDC-0919 (**200 mg**) + atezolizumab (1200 mg)	12
GDC-0919 (**400 mg**) + atezolizumab (1200 mg)	6
GDC-0919 (**600 mg**) + atezolizumab (1200 mg)	17
GDC-0919 (**1000 mg**) + atezolizumab (1200 mg)	18
Total number of patients in dose escalation groups	**66**

Dose expansion groups

- Patients in **Group A** got GDC-0919 as a single agent on Days 1-21 before starting their combination treatment on Day 22.
- Patients in **Group B** got atezolizumab as a single agent on Day 1 before starting their combination treatment on Day 22.
- In all **other groups**, patients took their GDC-0919 pill twice a day and received atezolizumab by IV, once every 3 weeks.
- Some patients joined groups according to the type of cancer they had: Non-small-cell lung cancer (**NSCLC**); kidney (renal) cell cancer (**RCC**); triple-negative breast cancer (**TNBC**); urinary bladder cancer (**UBC**).
- Patients joined **Relapse-1** group if they had received a single-agent treatment targeting the PD-L1 pathway and had responded to the treatment for at least 6 months before starting this study.
- Patients joined **Relapse-2** group if they had received a single-agent treatment targeting the PD-L1 pathway and had responded to the treatment for more than 6 weeks but not more than 6 months before starting this study.

Dose	Group	Number of patients
GDC-0919 (**600 mg**) + atezolizumab (1200 mg)	A-600	10
GDC-0919 (**1000 mg**) + atezolizumab (1200 mg)	A-1000	1
GDC-0919 (**600 mg**) + atezolizumab (1200 mg)	B-600	6
GDC-0919 (**1000 mg**) + atezolizumab (1200 mg)	B-1000	6
GDC-0919 (**600 mg**) + atezolizumab (1200 mg)	NSCLC-600	16
GDC-0919 (**1000 mg**) + atezolizumab (1200 mg)	NSCLC-1000	10
GDC-0919 (**600 mg**) + atezolizumab (1200 mg)	RCC-600	7
GDC-0919 (**1000 mg**) + atezolizumab (1200 mg)	TNBC-600	11
GDC-0919 (**600 mg**) + atezolizumab (1200 mg)	UBC-600	4
GDC-0919 (**1000 mg**) + atezolizumab (1200 mg)	UBC-1000	4
GDC-0919 (**600 mg**) + atezolizumab (1200 mg)	Relapse-1-600	7
GDC-0919 (**1000 mg**) + atezolizumab (1200 mg)	Relapse-1-1000	5
GDC-0919 (**600 mg**) + atezolizumab (1200 mg)	Relapse-2-600	3
GDC-0919 (**1000 mg**) + atezolizumab (1200 mg)	Relapse-2-1000	2
Total number of patients		**92**

What was done on the study

Patients were seen by their doctors on a regular basis, who collected patient samples for lab analyses and also did tests. Doctors found out how patients were reacting to the medicine. They took note of and treated any side effects.

How much medicine did patients get

Half of the patients received GDC-0919 for more than 51 days (median: 51; range: 1–889). Half of the patients received atezolizumab for more than 56 days (median: 56; range: 1–1208).

What happened to patients on the study

All 157 patients (99%) who got any amount of either medicine stopped their treatment. Most patients stopped taking GDC-0919 (102 patients, 65%) or atezolizumab (116 patients, 73%) because their disease became worse (disease progression).

4. What were the results of the study?

Question 1: Was it safe and could the side effects be tolerated when patients received treatment that combined GDC-0919 and atezolizumab?

The majority of patients (75%) reported side effects as a result of the combination treatment. Rash was observed in over a quarter (27%) of the patients; rash could be managed. This combination therapy was thought to be generally well tolerated.

Question 2: What was the largest dose of GDC-0919 that could be combined with a fixed dose of atezolizumab?

The largest dose of GDC-0919 given to patients was 1000 mg, twice a day, which was generally safe. Researchers did not go beyond this dose, so they did not find the dose that patients should not exceed.

Question 3: What happens to GDC-0919 and atezolizumab in the body when given as a combination treatment?

Researchers found out that each medicine was quickly absorbed into the body. The amount absorbed was related to the dose of the medicine. Researchers did not find any differences in what happened to each medicine when given to patients as single agents or as combination therapy.

Question 4: Does the combination treatment improve the outcome for patients when compared to studies where patients got these medicines as a single agent?

Results did not show any clear benefit that was gained by combining GDC-0919 with atezolizumab. Therefore, the Sponsor stopped the study and discontinued development of GDC-0919 in combination with atezolizumab.

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.

Common and serious side effects are listed below:

Most common side effects

During this study, a total of 117 patients (75%) had side effects thought to be caused by the study medicines.

- 113 patients (72%) had side effects thought to be caused by GDC-0919.

- 94 patients (60%) had side effects thought to be caused by atezolizumab.

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

Common side effects caused by either medicine	Number of patients (and percentages) who got this side effect
Feeling tired (fatigue)	37 (24%)
Unusual colored urine (chromaturia)	32 (20%)
Rash	27 (17%)
Feeling sick (nausea)	20 (13%)
Not hungry (decreased appetite)	19 (12%)
Vomiting	13 (8%)
Feeling weak (asthenia)	12 (8%)
Abnormal liver test results (aspartate aminotransferase increased)	12 (8%)
Diarrhea	10 (6%)
Fever (pyrexia)	9 (6%)
Decreased red blood cells (anemia)	9 (6%)
Pain in joints (arthralgia)	8 (5%)

Serious side effects

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

During this study, 16 patients (10%) reported having a total of 21 serious side effects thought to be related to any of the study medicines.

- Two patients had rash.
- There were 19 other serious side effects that were only reported a single time each.

Deaths

A total of 56 patient deaths (36%) were reported in this study.

- 53 patients (15%) died because when their cancer became worse (progressed).
- 1 patient died from breathing difficulties (respiratory failure) thought to be related to the study treatment.
- 1 patient died due to a brain injury (cerebrovascular accident) that was not related to the study treatment.
- 1 patient died from unknown reasons.

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 158 patients with several different kinds of cancer. These results helped researchers learn about the effects of combining GDC-0919 with atezolizumab.

The side effects of the combination of GDC-0919 and atezolizumab were generally manageable and well tolerated. However, there was no clear evidence of clinical benefit that was gained by combining GDC-0919 with atezolizumab. Therefore, the Sponsor stopped the study and discontinued development of GDC-0919 in combination with atezolizumab.

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?

There were several studies that were completed and others that were ongoing at the time this study was completed:

Studies for GDC-0919:
https://clinicaltrials.gov/ct2/results?cond=&term=GDC-0919&cntry=&state=&city=&dist=

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

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/NCT02471846

If you would like to find out more about the results of this study:

- The full title of the relevant scientific paper is:
  "Phase 1 study of the indoleamine 2,3-dioxygenase 1 (IDO1) inhibitor navoximod (GDC-0919) administered with PD-L1 inhibitor (atezolizumab) in advanced solid tumors".
- The authors of the scientific paper are:
  Kyung Hae Jung, Patricia LoRusso, Howard Burris, Michael Gordon, Yung-Jue Bang, and others.
- The paper is published in the journal:
  Clinical Cancer Research; volume number 25 (issue 11), on pages 3320 to 3328.

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 1b, open-label, dose-escalation study of the safety and pharmacology of GDC-0919 administered with atezolizumab in patients with locally advanced or metastatic solid tumors”.

- The protocol number for this study is GO29779.
- The ClinicalTrials.gov identifier for this study is NCT02471846.