

Summary of Clinical Trial

A study of atezolizumab, when taken alone or with other medicines, in people with multiple myeloma (a type of cancer that affects the bone marrow in various parts of 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 (called a 'study' in this document) – written for:

- the people who took part in the study, and
- members of the public.

This summary is based on information known at the time that it was written.

Contents of the summary

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2. Who took part in this study?
3. What happened during the study?

The study started in July 2015 but stopped early because the medicines being studied did not work as well as expected. 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.**

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4. What were the results of the study?
 5. What were the side effects?
 6. How has this study helped research?
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Glossary

- Multiple myeloma (MM) = a type of cancer that affects the bone marrow in various parts of the body
- Bone marrow = a soft, spongy tissue that is found in the center of most bones and is where most blood cells are made
- Relapsed or refractory = the cancer has come back after being treated or did not get better with the previous treatment
- Treatment cycle = a period in which treatment is given, followed by a rest period where no treatment is given. (For example, one treatment cycle = 1 week of treatment followed by 3 weeks of rest.) Treatment cycles are generally repeated on a regular schedule.

Thank you to the people who took part in this study

As a clinical study participant, you belong to a large community of people around the world who have made it possible for researchers to answer important scientific questions about a type of cancer that affects the bone marrow in various parts of the body (called ‘multiple myeloma’) and the medicines studied – ‘atezolizumab’, ‘daratumumab’, ‘lenalidomide’ and ‘pomalidomide’.

Thank you for taking part in this clinical study and for giving us your time.

As the company that has organized and funded this study (Sponsor), we believe it is important for you to know the results of this study. We hope it helps you understand and feel proud of the critical role you have played in medical research. If you have questions about the results outlined in this document, please speak with the study researcher, research nurse, or other team members at your study site.

It is also important to remember that one study cannot tell us everything about the possible side effects of a drug and how well it may work. It takes a lot of people in many studies to learn as much as we can about medicines like atezolizumab, daratumumab, lenalidomide and pomalidomide. The results of this study may be different from the

results of other studies of these drugs. This means that you should not make medical decisions based on this one summary. Always talk to your doctor before making any decisions about your treatment.

1. General information about this study

Why was this study done?

Multiple myeloma is a type of cancer that affects the bone marrow in various parts of a person's body. People with multiple myeloma may be given several different types of treatment, including:

- **Chemotherapy** – medicines that use powerful chemicals to kill all fast-growing cells, such as cancer cells, in the body;
- **Immunotherapy** – medicines that stimulate the body's immune system to kill cancer cells; and/or
- **Bone marrow transplant** – a procedure where healthy stem cells that produce blood are infused into the body to replace unhealthy or damaged bone marrow. An 'autologous stem cell transplant' is a bone marrow transplant that uses cells from the patient's own body – rather than from a donor.

The people in this study had previously been given medicines or a bone marrow transplant for multiple myeloma, but the cancer came back after treatment, or these treatments did not work (this is called 'relapsed or refractory multiple myeloma').

This study looked to see if combinations of several new medicines were safe and may work for people with relapsed or refractory multiple myeloma.

What medicines were used to treat people in this study?

This study looked at several different combinations of medicines for the treatment of multiple myeloma. That's because taking two or more medicines that work in different ways to treat cancer may work better than taking a single medicine. (Combination therapy is commonly used to treat multiple myeloma.)

Atezolizumab was the main medicine that was studied. The other medicines studied were daratumumab, lenalidomide and pomalidomide – these are existing medicines that are already approved for the treatment of multiple myeloma that were used in combination with atezolizumab in this study.

'Atezolizumab' is the main medicine in this study

- You pronounce this as 'a-teh-zo-LIZ-oo-mab'.
- The body's immune system fights diseases like cancer, but sometimes cancer cells can block (stop) the immune system from attacking the cancer. Atezolizumab may release this blockage – meaning that the immune system again becomes able to fight the cancer cells.
- When people take atezolizumab, their cancer may be reduced.
- This medicine is a type of 'immunotherapy' – medicine used in cancer to encourage the body's immune system to attack cancer cells.

'Daratumumab' is an existing medicine given to people with multiple myeloma.

- You pronounce this as 'DAYR-uh-TOOM-yoo-mab'.
- Daratumumab is a type of medicine that helps the immune system recognise and destroy multiple myeloma cancer cells.

'Lenalidomide' is an existing medicine given to people with multiple myeloma.

- You pronounce this as 'leh-nuh-LIH-doh-mide'.
- Lenalidomide is a medicine used to encourage the body's immune system to attack the multiple myeloma cancer cells.

'Pomalidomide' is an existing medicine given to people with multiple myeloma.

- You pronounce this as 'PAH-muh-LIH-doh-mide'.
- Pomalidomide is a medicine used to encourage the body's immune system to attack the multiple myeloma cancer cells.

'Dexamethasone' is an existing medicine given to people with multiple myeloma. It was used to treat the group of people in this study who did not receive atezolizumab (called a 'control group').

- You pronounce this as 'DEK-suh-MEH-thuh-son'.
- Dexamethasone is a type of steroid medicine that decreases the activity of the immune system. Dexamethasone can also increase the ability of other medicines to destroy myeloma cells.

What did researchers want to find out?

- Researchers did this study to see how well atezolizumab – when used by itself or in combination with various other medicines – worked to treat multiple myeloma (see section 4 "What were the results of the study?").

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- They also wanted to find out how safe the medicines were – by checking how many people experienced side effects and how serious these side effects were when taking the medicines during this study (see section 5 “What were the side effects?”).

The main questions that researchers wanted to answer were:

1. How well does atezolizumab work – when given by itself or in combination with other medicines – to treat multiple myeloma that has been previously treated? Does it reduce the amount of cancer or how much the disease will progress?
2. What side effects do people with multiple myeloma have when treated with atezolizumab plus other medicines (including daratumumab, lenalidomide and pomalidomide)?

What kind of study was this?

This study was a ‘Phase 1b’ study, which means that it was one of the first studies of atezolizumab in people with multiple myeloma. A small number of people took atezolizumab alone or in combination with other medicines. The researchers did medical tests on the people who took part in the study to find out more about atezolizumab when used with other study medicines.

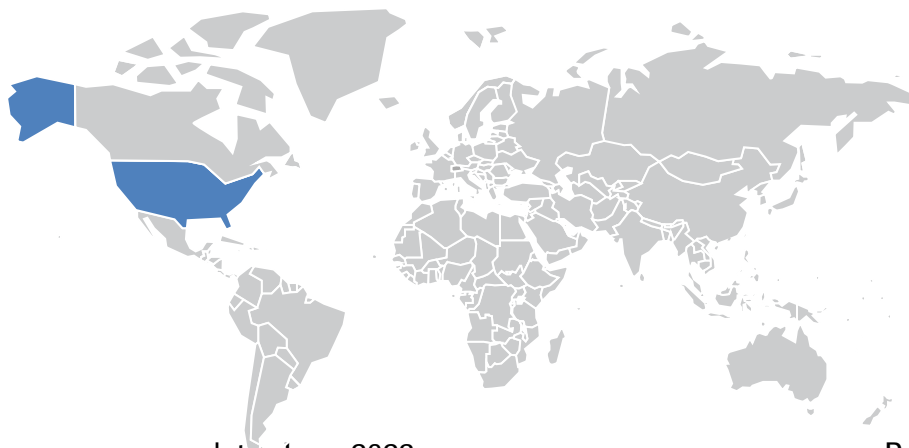
Participants in this study were placed into groups.

- The study used an ‘open label’ design for most groups, which means that both the people taking part in the study and the study researchers knew which of the study medicines people were taking.
- The study was ‘randomized’ for two groups – Groups F2 and F3. This means that it was decided by chance which of the study medicines people in these groups would have. Randomly choosing which medicine people take makes it more likely that the types of people in both groups will be a similar mix (for example, similar ages, similar races).
- Apart from the different medicines being tested, all other aspects of care were the same between the groups.

When and where did the study take place?

The study started in July 2015 and finished in March 2021. This summary was written after the study had ended.

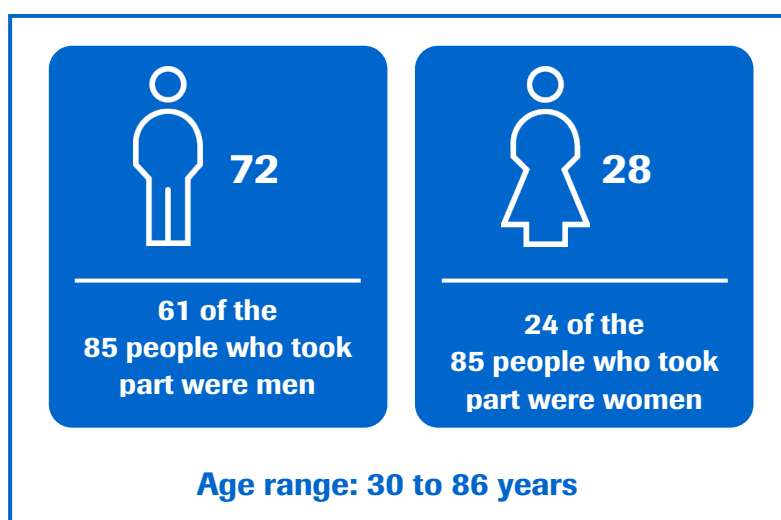
The study took place at 16 study centres across the United States.



2. Who took part in this study?

In total, 85 people with multiple myeloma took part in this study.

More information on the people who took part is given below.



People could take part in the study if:

- They had multiple myeloma that had come back after being treated or did not get better with previous treatment.
- They were 18 years of age or older.
- They were well enough to be able to look after themselves.

People could not take part in the study if they had had:

- Certain treatments or certain severe side effects from treatments for their multiple myeloma.
- A type of cancer other than multiple myeloma in the past 2 years (except very low-risk cancers).
- Previous treatment with atezolizumab or certain other medicines used in cancer to encourage the body's immune system to attack tumours.
- Uncontrolled cancer pain.
- Certain illnesses where the immune system attacks the body (autoimmune disease).

3. What happened during the study?

During the study, people were selected to get specific combinations of medicines, as noted below.

- **Groups A, B and E** were made up of people with multiple myeloma who had received up to three types of treatments or treatment combinations that did not work for them, or the cancer came back after treatment.
- **Group C** was made up of people with multiple myeloma who had evidence of disease after having a bone marrow transplant.
- **Group D** was made up of 3 subgroups of people with multiple myeloma – D1, D2 and D3.
 - People in **Groups D1 and D2** had received up to three types of treatments or treatment combinations that did not work for them, or the cancer came back after treatment.
 - People in **Group D3** had received at least two types of treatments or treatment combinations that did not work for them, or the cancer came back after treatment. In addition, their multiple myeloma was progressing during treatment with a type of medicine that helps the immune system to recognise the cancer.
- **Group F** was made up of people with multiple myeloma who had received four or more types of treatments or treatment combinations that did not work for them, or the cancer came back after treatment.

The groups received the following treatments:

Group A (6 people)	Atezolizumab by drip (infusion) into a vein
Group B (9 people)	Atezolizumab by drip (infusion) into a vein PLUS lenalidomide capsules by mouth
Group C (9 people)	Atezolizumab by drip (infusion) into a vein PLUS lenalidomide capsules by mouth
Group D (36 people)	Atezolizumab by drip (infusion) into a vein PLUS daratumumab by drip (infusion) into a vein.
Group E (7 people)	Atezolizumab by drip (infusion) into a vein PLUS daratumumab by drip (infusion) into a vein PLUS lenalidomide capsules by mouth
Group F1 and F2 (12 people – 6 people in F1 and 6 people in F2)	Atezolizumab by drip (infusion) into a vein PLUS daratumumab by drip (infusion) into a vein PLUS pomalidomide capsules by mouth
Group F3 (6 people)	Daratumumab by drip (infusion) into a vein PLUS pomalidomide capsules and dexamethasone tablets by mouth. (Group F3 did not receive atezolizumab, as this was a control group for the study doctors to compare to Group F2.)

The medicines in this study were given in ‘treatment cycles’.

- Each treatment cycle lasted for 3 or 4 weeks (depending on the group).
- People took the study medicines on particular days of the treatment cycle (and took no study medicines on other days in the cycle).

The study stopped early because the combination of medicines used did not work as well as expected.

4. What were the results of the study?

Question 1: How well does atezolizumab work – when given by itself or in combination with other medicines – to treat multiple myeloma that has been previously treated? Does it reduce the amount of cancer or how much the disease will progress?

Researchers collected information on the number of people in each group who responded to atezolizumab (either alone or in combination with other treatments) – in terms of tumour load and how much their multiple myeloma had progressed. This was monitored at various stages through the study with regular tests (such as blood tests, urine tests and X-rays).

The number of people from each group who responded to treatment are shown below.

Group	Number of people who responded
Group A (6 people)	None of the people responded
Group B (9 people)	1 of 9 people (11%) responded
Group C (9 people)	1 of 9 people (11%) responded
Group D (36 people)	In Group D1 , 4 of 6 people (67%) responded In Group D2 , 5 of 15 people (33%) responded In Group D3 , none of the people responded
Group E (7 people)	4 of 7 people (57%) responded
Group F1 and F2 (12 people – 6 people in F1 and 6 people in F2)	In Group F1 , 5 of 6 people (83%) responded In Group F2 , 3 of 6 people (50%) responded
Group F3 (6 people)	5 of 6 people (83%) responded

Question 2: What side effects do people with multiple myeloma have when treated with atezolizumab plus other medicines (including daratumumab, lenalidomide and pomalidomide)?

Researchers asked people about any side effects – such as nausea or the urge to vomit – that happened during the study. People in the study also had regular blood tests, measurements of body temperature, pulse rate and blood pressure.

The overall finding was that people who took part in this study did not have side effects that the researchers were not expecting them to have. These side effects were noted in other studies where the same medicines had been taken as a single medicine.

There is more information about side effects in Section 5.

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).

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 researcher believed the side effects were related to the treatments in the study.
- Not all of the people 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.

During this study, 17 out of 85 people (20%) had at least one serious side effect.

- None of the people in **Groups A, B or C** had a serious side effect.
- **Group D** – 5 out of 36 people (14%) had a serious side effect.
- **Group E** – 3 out of 7 people (43%) had a serious side effect.
- **Group F1 and F2** – 6 of 12 people (50%) had a serious side effect.
- **Group F3** – 3 of 6 people (50%) had a serious side effect.

The serious side effects are shown in the following tables – these are all of the serious side effects across all treatment groups. Some people had more than one side effect – this means that they are included in more than one row in the table.

Serious side effects reported in this study (Groups A, B C, D, E)	Groups A, B and C atezolizumab alone or with lenalidomide (24 people total)	Group D atezolizumab and daratumumab (36 people total)	Group E atezolizumab and daratumumab and lenalidomide (7 people total)
Lung infection (pneumonia)	0	6% (2 out of 36)	14% (1 out of 7)
Low levels of platelets (fragments of blood that help blood to clot) – known as thrombocytopenia	0	0	14% (1 out of 7)
Fever with a low level of white blood cells	0	0	14% (1 out of 7)
Disease affecting the blood vessels to the heart (coronary artery disease)	0	3% (1 out of 36)	0
Heart attack	0	3% (1 out of 36)	0
An immune system reaction to the study medicine being given by a drip into the vein (infusion-related reaction)	0	3% (1 out of 36)	0
Fever	0	3% (1 out of 36)	0
Inflammation of the pancreas	0	0	14% (1 out of 7)
Inflammation of the liver related to the immune system	0	0	14% (1 out of 7)

Serious side effects reported in this study (Group F)	Groups F1 and F2 atezolizumab and daratumumab and pomalidomide (12 people total)	Group F3 daratumumab and pomalidomide and dexamethasone (6 people total)
Lung infection (pneumonia)	33% (4 out of 12)	33% (2 out of 6)
Fever with a low level of white blood cells	17% (2 out of 12)	0
Flu	8% (1 out of 12)	0
Inflammation of the lymph nodes	8% (1 out of 12)	0

Skin infection	0	17% (1 out of 6)
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During the study, some people decided to stop taking their medicine because of side effects.

- In **Groups A, B and C**, nobody stopped taking their medicine(s) because of side effects.
- In **Group D**, 1 out of 36 people (3%) stopped taking their medicine.
- In **Group E**, 1 out of 7 people (14%) stopped taking their medicine.
- In **Groups F1 and F2**, 2 out of 12 people (17%) stopped taking their medicine.
- In **Group F3**, 1 out of 6 people (17%) stopped taking their medicine.

Most common side effects

Most people in this study had a side effect. Most side effects were not considered serious and serious side effects have been described in the previous section.

- 55 of 79 people (70%) who were given atezolizumab had a side effect from atezolizumab.
- 15 of 25 people (60%) who were given lenalidomide had a side effect from lenalidomide.
- 51 of 61 people (84%) who were given daratumumab had a side effect from daratumumab.
- 17 of 18 people (94%) who were given pomalidomide had a side effect from pomalidomide.
- 4 of 6 people (67%) who were given dexamethasone had a side effect from dexamethasone.

The most common side effects are shown in the following tables – these are the 3 most common side effects across each treatment group. Some people had more than one side effect – this means that they are included in more than one row in the table.

Most common side effects from atezolizumab reported in this study			
	Fatigue	Low levels of platelets (fragments of blood that help blood to clot) – known as thrombocytopenia	Fever
Group A	0	0	17% (1 out of 6)
Group B	0	22% (2 out of 9)	0
Group C	22% (2 out of 9)	0	0
Group D	19% (7 out of 36)	8% (3 out of 36)	3% (1 out of 36)
Group E	0	29% (2 out of 7 patients)	29% (2 out of 7)

Groups F1 and F2	33% (4 out of 12)	8% (1 out of 12)	0
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Most common side effects from daratumumab reported in this study			
	Low levels of white blood cells	Low levels of platelets (fragments of blood that help blood to clot) – known as thrombocytopenia	Diarrhoea
Group D	17% (6 of 36)	11% (4 out of 36)	11% (4 out of 36)
Group E	14% (1 out of 7)	43% (3 out of 7)	0
Group F1 and F2	50% (6 out of 12)	25% (3 out of 12)	0
Group F3	33% (2 out of 6)	0	50% (3 out of 6)

Most common side effects from pomalidomide reported in this study			
	Low levels of white blood cells	Fatigue	Diarrhoea
Group F1 and F2	67% (8 out of 12)	50% (6 out of 12)	42% (5 out of 12)
Group F3	50% (3 out of 6)	33% (2 out of 6)	33% (2 out of 6)

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 85 people with multiple myeloma. These people had received previous medicines for their cancer, but the medicines did not work, or the cancer came back.

The results of this study have helped researchers learn more about multiple myeloma and about the medicine atezolizumab, when used together with other medicines for the treatment of multiple myeloma.

This study looked at whether it was safe to give people with multiple myeloma different combinations of medicines with atezolizumab. It also looked at whether these

combinations of medicines worked to treat multiple myeloma that had come back after being treated or did not get better with previous treatment.

People in this study did not have side effects that the researchers were not expecting them to have. These side effects were noted in other studies where the same medicines had been taken as a single medicine.

Unfortunately, the combinations of treatments in this study did not work as well as expected. As a result, the combinations studied will not likely be further developed for use in people with relapsed or refractory multiple myeloma.

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?

At the time of writing this summary, no more studies looking at atezolizumab (plus other medicines) are planned in people with multiple myeloma.

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/study/NCT02431208>
- <https://forpatients.roche.com/en/trials/cancer/multiple-myeloma/a-study-of-atezolizumab--anti-programmed-death-ligand-1--pd-l1--.html>

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/trials/cancer/multiple-myeloma/a-study-of-atezolizumab--anti-programmed-death-ligand-1--pd-l1--.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 organised and paid for this study?

This study was organised and paid for by F. Hoffmann-La Roche Ltd who have their headquarters in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study is: “A phase 1b study of the safety and pharmacokinetics of atezolizumab (anti-PD L1 antibody) alone or in combination with an immunomodulatory drug and/or daratumumab in patients with multiple myeloma (relapsed/refractory) and post autologous stem cell transplantation”.

- The protocol number for this study is: GO29695.
The ClinicalTrials.gov identifier for this study is: NCT02431208.