

Summary of Clinical Trial Results

A study of atezolizumab, in combination with either obinutuzumab or rituximab, in people with certain types of non-Hodgkin's lymphoma (cancer of the lymph nodes)

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:

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

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

The study started in December 2017 and finished in January 2022. 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

1. General information about this study
2. Who took part in this study?
3. What happened during the study?
4. What were the results of the study?
5. What were the side effects?
6. How has this study helped research?
7. Are there plans for other studies?
8. Where can I find more information?

Glossary

- NHL = cancer of the lymph nodes called 'non-Hodgkin's lymphoma'
Three types of NHL are:
- MCL = Mantle cell lymphoma
- MZL = Marginal zone lymphoma
- WM = Waldenström's macroglobulinemia
- 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 repeated on a regular schedule.

Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about three types of cancer of the lymphatic system called 'non-Hodgkin's lymphoma (or NHL) and the medicines studied – 'atezolizumab', 'obinutuzumab' and 'rituximab'.

1. General information about this study

Why was this study done?

Non-Hodgkin's lymphoma (NHL) is a cancer of the lymph nodes. In this type of cancer, white blood cells grow abnormally and form tumours throughout the body. NHL is one of the leading causes of cancer death in both the United States and Europe.

There are different types of NHL including **mantle cell lymphoma (MCL)**, **marginal zone lymphoma (MZL)** and **Waldenström's macroglobulinemia (WM)**.

People with MCL, MZL or WM may be given different types of treatment, including:

- chemotherapy (medicines to kill cancer); and
- immunotherapy (medicines that stimulate the body's own immune system to kill cancer cells).

The people in this study had previously been given medicine for MCL, MZL or WM, but this medicine did not work, or the cancer came back after treatment (relapsed or refractory lymphoma).

This study looked at whether a new combination of medicines may work and is safe for people with relapsed or refractory MCL, MZL or WM.

What were the study medicines?

This study looked at two different combinations of medicines for the treatment of NHL. Combination therapy is when two or more medicines are given together. Combination therapy is commonly used to treat NHL.

Atezolizumab was the main medicine that was studied. The other medicines studied were obinutuzumab and rituximab – these are existing medicines, but in this study they were used in combination with atezolizumab.

'Atezolizumab' is the main medicine that was studied here.

- You say this as 'a – teh – zo – liz – oo – mab'.
- This medicine is a type of 'immunotherapy' – medicine used in cancer to encourage the body's immune system to attack cancer cells.
- 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 is able to fight the cancer cells.
- When people take atezolizumab, their cancer may shrink.
- Atezolizumab is an existing medicine given to people with different cancers, such as lung cancer.

'Obinutuzumab' is an existing medicine given to people with some types of lymphoma.

- You say this as ‘oh – bin – oo – too – zoo – mab’.
- It is a type of immunotherapy that attaches to the surface of certain white blood cells called B cells and tells the body’s immune system to attack and destroy those cells. Obinutuzumab is expected to kill cancerous B cells.

‘Rituximab’ is an existing medicine given to people with some types of lymphoma in combination with chemotherapy.

- You say this as ‘ri – tux – i – mab’.
- It is another type of immunotherapy that attaches itself to certain B cells and tells the body’s immune system to attack and destroy those cells. Rituximab is expected to kill the cancerous B cells.

What did researchers want to find out?

- Researchers did this study to find out how well atezolizumab and obinutuzumab worked to treat MCL and WM, and to find out how well atezolizumab and rituximab worked to treat MZL (see section 4 “What were the results of the study?”).
- They also wanted to find out how safe the medicines were – by checking how many people had side effects and seeing 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 many people with MCL or WM had smaller or no tumours after treatment with atezolizumab and obinutuzumab?
2. How many people with MZL had smaller or no tumours after treatment with atezolizumab and rituximab?

What kind of study was this?

This study was a ‘Phase 2’ study. This means that atezolizumab, obinutuzumab and rituximab had all been tested in a number of people with advanced lymphoma before this study.

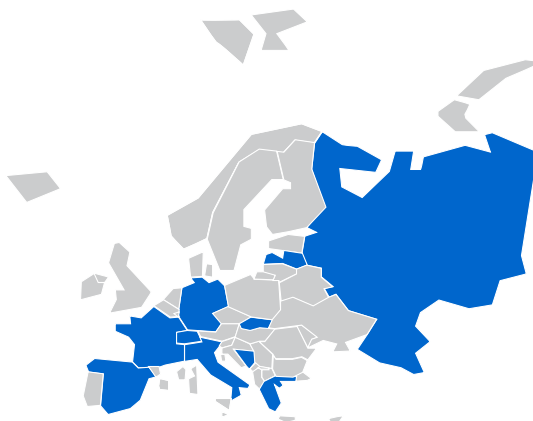
The researchers wanted to find out more about atezolizumab when it is used in combination with the other study medicines. This was an open-label study. This means that both the people taking part in the study and the study doctors knew what amount of atezolizumab, obinutuzumab and rituximab people were taking.

When and where did the study take place?

The study started in November 2017 and finished in January 2022. This summary was written after the study had ended.

The study took place at 21 study centres across 10 countries in Europe. The following map shows the countries where this study took place.

- *Bosnia & Herzegovina*
- *France*
- *Germany*
- *Greece*
- *Italy*
- *Latvia*
- *Russia*
- *Slovakia*
- *Spain*
- *Switzerland*



2. Who took part in this study?

People could take part in the study if:

- They were at least 18 years old
- The cancer had come back after treatment or did not get better with treatment
- The cancer was able to be measured through tests or other imaging
- They were well enough to look after themselves

People could **not** take part in the study if:

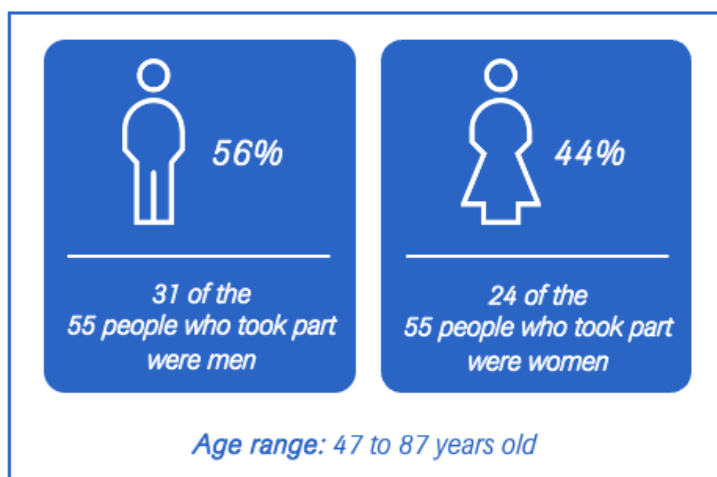
- They had lymphoma that had spread to the brain or spinal cord
- They had taken any other anticancer therapy within the 3 weeks before starting the study
- They had taken any other clinical trial medicines within the 4 weeks before starting the study
- They had an illness where the immune system attacks their own body (autoimmune disease)

Altogether, 55 people took part in the study. There were:

- 30 people with MCL
- 21 people with MZL
- 4 people with WM

People who took part in the study were aged between 47 and 87 years old. Of the 55 people in the study, 31 (56%) were male and 24 (44%) were female.

All the people in the study had received previous treatment for their lymphoma.



3. What happened during the study?

People were given atezolizumab and obinutuzumab or atezolizumab and rituximab depending on the type of lymphoma they had.

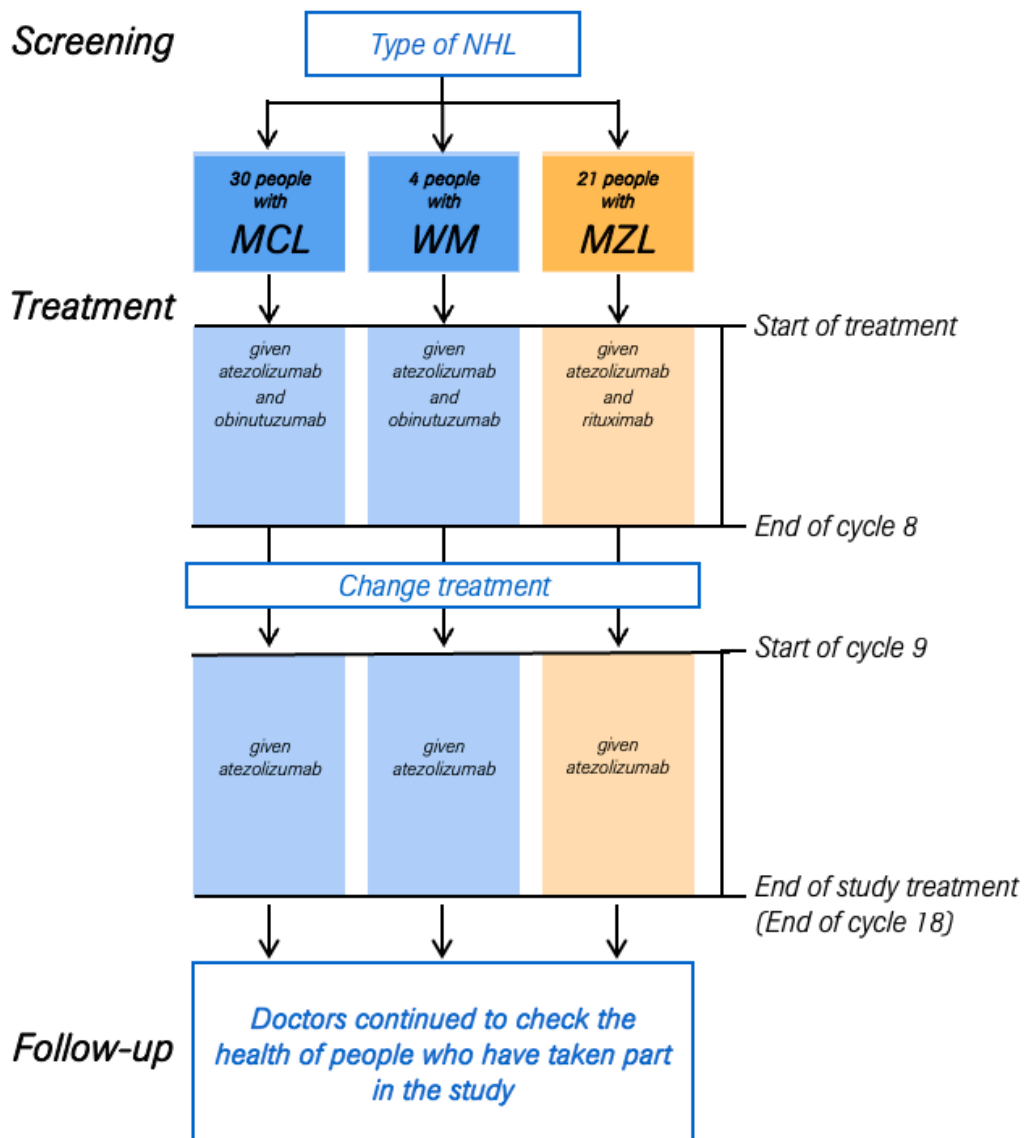
- **People with MCL or WM** were given atezolizumab and obinutuzumab. Both medicines were given by drip (infusion) into a vein
- **People with MZL** were given atezolizumab and rituximab. Atezolizumab was given by drip (infusion) into a vein. Rituximab was given by a drip (infusion) into a vein the first time, but after that it was given as an injection under the skin.

The medicines in this study were given in ‘treatment cycles.’ This means that medicines were given on a schedule that was repeated. Each treatment cycle lasted 3 weeks.

- **People with MCL or WM** were given atezolizumab on Day 1 and obinutuzumab on Day 1, Day 8 and Day 15 of the first treatment cycle. From the second treatment cycle, people with MCL or WM received atezolizumab and obinutuzumab on Day 1 of each treatment cycle.
- **People with MZL** were given atezolizumab and rituximab on Day 1 of each treatment cycle.
- After the first 8 treatment cycles, people stopped taking obinutuzumab or rituximab.
- For the next 10 cycles, people in the study took only atezolizumab on Day 1 of each cycle

People stopped taking the study medicines early if their cancer got worse, or if they or their doctor decided they should stop because of the side effects of the medicines.

When the study finished, the people who took part were asked to go back to their study centre for more visits – to check their overall health. See below for more information about what happened in the study.



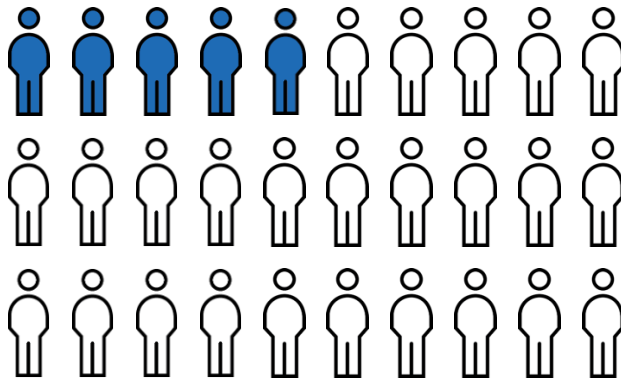
4. What were the results of the study?

The results of the study are shown for each question.

Question 1: How many people with MCL or WM had smaller or no tumours after treatment with atezolizumab and obinutuzumab?

The researchers looked at how many people had smaller or no tumours during the study – compared to the start of the study.

- For the people with MCL – 5 out of 30 people (17%) had smaller or no tumours
- For the people with WM – 0 out of 4 people (0%) had smaller or no tumours

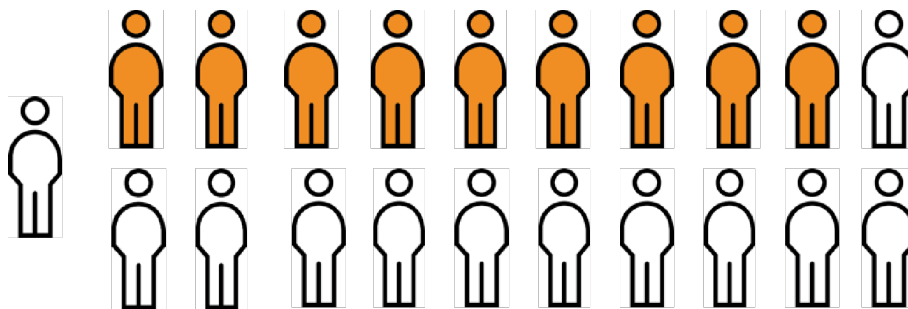


5 out of 30 people (17%) with MCL had cancers that shrunk or disappeared after being given atezolizumab and obinutuzumab

Question 2: How many people with MZL had smaller or no tumours after treatment with atezolizumab and rituximab?

The researchers looked at how many people had smaller or no tumours during the study – compared to the start of the study.

- For the people with MZL - 9 out of 21 people (43%) had smaller or no tumours



9 out of 21 people (43%) with MZL had cancers that shrunk or disappeared after being given atezolizumab and rituximab

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 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 side effects

Researchers consider a side effect to be 'serious' if it is life-threatening, needs hospital care, or causes lasting problems.

Serious side effects are shown in the following tables. Some people had more than one side effect – this means that they are included in more than one row in the table.

During this study, some people had a serious side effect from **atezolizumab**:

- 5 out of 30 people (17%) with MCL had a serious side effect from atezolizumab
- 3 out of 21 people (14%) with MZL had a serious side effect from atezolizumab
- No-one with WM had a serious side effect

Serious side effects from atezolizumab reported in this study	People with MCL (30 people)	People with WM (4 people)	People with MZL (21 people)
Lung infection (pneumonia)	3% (1 out of 30)	0%	0%
Inability of the heart to pump enough oxygen to the body (cardiac failure)	3% (1 out of 30)	0%	0%
A viral infection (cytomegalovirus)	3% (1 out of 30)	0%	0%
Fluid collecting in the abdomen	3% (1 out of 30)	0%	0%
Low levels of a type of white blood cells (neutrophils)	3% (1 out of 30)	0%	0%
Not enough red blood cells (anaemia)	0%	0%	5% (1 out of 21)
Fever associated with low levels of a type of white blood cell (neutrophils)	0%	0%	5% (1 out of 21)
Severe illness from bacteria in the blood stream	0%	0%	5% (1 out of 21)
Skin irritation caused by an allergic reaction	0%	0%	5% (1 out of 21)

During this study, some people had a serious side effect from **obinutuzumab**:

- 3 out of 30 people (10%) with MCL had a serious side effect from obinutuzumab
- No-one with WM had a serious side effect

Serious side effects from obinutuzumab reported in this study	People with MCL (30 people)	People with WM (4 people)
Lung infection (pneumonia)	3% (1 out of 30)	0%
Severe illness from bacteria in the blood stream	3% (1 out of 30)	0%
Inability of the heart to pump enough oxygen to the body (cardiac failure)	3% (1 out of 30)	0%
A viral infection (cytomegalovirus)	3% (1 out of 30)	0%

During this study, some people had a serious side effect from rituximab

- 4 out of 21 people (19%) with MZL had a serious side effect from rituximab

Serious side effects from rituximab reported in this study	People with MZL (21 people total)
Fever	5% (1 out of 21)
Fever associated with low levels of a type of white blood cell (neutrophils)	5% (1 out of 21)
Severe illness from bacteria in the blood stream	5% (1 out of 21)
Not enough red blood cells (anaemia)	5% (1 out of 21)
Skin irritation caused by an allergic reaction	5% (1 out of 21)

No-one in the study died due to side effects that were related to one of the study medicines.

During the study, some people decided to stop taking one or both of the study medicines because of side effects:

- 2 out of the 30 people (7%) with MCL stopped taking atezolizumab and obinutuzumab.
- 4 out of 21 people (19%) with MZL stopped taking atezolizumab and rituximab.

Common side effects

The most common side effects are shown in the following tables – these are the side effects experienced by **at least 1 in 10 people (10%)** with each type of NHL. Some people had more than one side effect – this means that they are included in more than one row in the table.

During this study, some people had at least 1 side effect from **atezolizumab**:

- 19 out of 30 people (63%) with MCL had a side effect from atezolizumab.
- 3 out of 4 people (75%) with WM had a side effect from atezolizumab.
- 15 out of 21 people (71%) with MZL had a side effect from atezolizumab.

Most common side effects from atezolizumab reported in this study	People with MCL (30 people)	People with WM (4 people)	People with MZL (21 people)
Low levels of white blood cells (neutrophils)	20% (6 out of 30)	50% (2 out of 4)	14% (3 out of 21)
Low levels of red blood cells (anaemia)	10% (3 out of 30)	0%	14% (3 out of 21)
*Low levels of platelets (blood cell fragments that help blood to clot)	13% (4 out of 30)	25% (1 out of 4)	0%
*A blood disorder from low levels of platelets (blood cell fragments that help blood to clot)	10% (3 out of 30)	25% (1 out of 4)	0%
Joint pain	0% (0 out of 30)	25% (1 out of 4)	14% (3 out of 21)

*These are very similar side effects, but they are measured in different ways.

During this study, some people had at least 1 side effect from **obinutuzumab**:

- 18 out of 30 people (60%) with MCL had a side effect from obinutuzumab.
- 3 out of 4 people (75%) with WM had a side effect from obinutuzumab.

Most common side effects from obinutuzumab reported in this study	People with MCL (30 people)	People with WM (4 people)
*Low levels of platelets (blood cell fragments that help blood to clot)	17% (5 out of 30)	50% (2 out of 4)
*A blood disorder from low levels of platelets (blood cell fragments that help blood to clot)	17% (5 out of 30)	25% (1 out of 4)
Low levels of a type of white blood cells (neutrophils)	17% (5 out of 30)	25% (1 out of 4)
Low levels of red blood cells (anaemia)	13% (4 out of 30)	0%

*These are very similar side effects, but they are measured in different ways.

During this study, some people had at least 1 side effect from **rituximab**:

- 17 out of 21 people (81%) with MZL had a side effect from rituximab

Most common side effects from rituximab reported in this study	People with MZL in Group B (21 people total)
Low levels of red blood cells (anaemia)	14% (3 out of 21)
Low levels of a type of white blood cells (neutrophils)	14% (3 out of 21)
Joint pain	14% (3 out of 21)

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 55 people with certain types of NHL (MCL, MZL, WM). 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 what happens when certain types of NHL are treated with the medicine atezolizumab used together with obinutuzumab or rituximab.

This study looked at whether these combinations of medicines worked for people with MCL, MZL or WM, and for how long. It also looked at whether it was safe to give people with MCL, MZL or WCM these combinations of medicines.

The study has shown that:

- Almost half of the people with MZL had smaller or no tumours after they had been given atezolizumab and rituximab.
- Some people with MCL had smaller or no tumours after they had been given atezolizumab and obinutuzimab.
- None of the four people with WM had smaller or no tumours after they had been given atezolizumab and obinutuzimab.

In this study, the most common side effects from the study medicines were low levels of white blood cells (neutrophils), low levels of red blood cells (anaemia), low levels of platelets (blood cell fragments that help blood to clot) and joint pain.

People in this study did not have side effects that the researchers were not expecting them to have.

No single study can tell us everything about the risks and benefits of a medicine. It takes a lot 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 medicines.

- **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?

This study on atezolizumab in combination with obinutuzumab or rituximab is finished. No further studies are planned with these combinations of medicines.

8. Where can I find more information?

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

- <https://www.clinicaltrialsregister.eu/ctr-search/trial/2016-003579-22/SK>
- <https://forpatients.roche.com/en/trials/cancer/a-study-exploring-the-safety-and-efficacy-of-atezolizumab-in-com.html>

If you would like to find out more about the results of this study, you may want to read the relevant scientific paper.

- The full title of the paper is: “A phase-II study of atezolizumab in combination with obinutuzumab or rituximab for relapsed or refractory mantle cell or marginal zone lymphoma or Waldenström’s macroglobulinemia”.
- The authors of the scientific paper are Panayiotis Panayiotidis, Gayane Tumyan, Catherine Thieblemont, Vadim V. Ptushkin, Ana Marin-Niebla, Ramon García-Sanz, and others.
- The paper is published in the journal: ‘Leukemia & Lymphoma’, volume number 63 issue 5, on pages 1058-1069.

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/a-study-exploring-the-safety-and-efficacy-of-atezolizumab-in-com.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 II Study Exploring the Safety and Efficacy of Atezolizumab Administered in Combination with Obinutuzumab or Rituximab Anti-CD20 Therapy in Patients with Relapsed/Refractory Mantle Cell Lymphoma, Marginal Zone Lymphoma and Waldenström Macroglobulinemia”.

- The study is known as ‘TeGAR’.
- The protocol number for this study is: MO39107
- The EudraCT number for this study is: 2016-003579-22.