# Summary of Clinical Trial Results

## A study to look at whether it is safe to shorten the infusion duration of obinutuzumab in patients with follicular lymphoma (a type of cancer of the lymphatic system)

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 February 2019. This summary includes the final results that were collected and analysed by April 2023. At the time of writing this summary, the study has been completed – patients are no longer treated in this study and study doctors are no longer collecting information.

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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### Glossary

- Non-Hodgkin's lymphoma (NHL) = cancer of the lymph nodes.
- Follicular lymphoma (FL) = the most common type of NHL.

## Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about a cancer of the lymphatic system called 'follicular lymphoma' or 'FL', and the medicine studied – obinutuzumab.

## Key information about this study

- This study was done to look for a different way to treat a certain type of cancer called "follicular lymphoma".
- This study included 113 people in 7 countries.
- In this study, people were given the medicine being studied (called obinutuzumab). Researchers wanted to find out if it is safe to infuse obinutuzumab faster into patients' veins when they are being treated for follicular lymphoma. Researchers looked at all possible side effects of obinutuzumab but they specifically focused on side effects that appear during the infusion of obinutuzumab or in the next 24 hours after the infusion. These specific types of side effects are known as "Infusion-related reactions" or IRRs.
- Looking at IRRs, the study has shown that approximately 1 in 100 people had a serious IRR with a faster intravenous infusion (drip into a vein) of obinutuzumab. About 20 in 100 people had a mild to moderate IRR, and 79 in 100 people had no IRR from having a faster intravenous infusion (drip into a vein) of obinutuzumab.
- Looking at all side effects over the whole study duration, even weeks or months after the infusion of obinutuzumab, around 99% of people (112 out of 113) had at least one side effect that may or may not have been related to taking obinutuzumab. Out of these, 90% of people (102 out of 113) had side effects that doctors believed to be related to taking obinutuzumab.
- Over the whole study duration, around 40% of people (45 out of 113) had serious side effects that may or may not have been related to taking obinutuzumab.
- At the time of writing this summary, the study has been completed.

## 1. General information about this study

### Why is this study being done?

Researchers were looking for a different way to treat a certain type of cancer of the lymphatic system called follicular lymphoma, or FL. The lymphatic system is an important part of the immune system (it includes, for example, the lymph nodes and the spleen). People with FL have higher levels of abnormal B cells in their body. B cells are a type of white blood cells. All the patients in the study had follicular lymphoma (FL) that had not been treated yet.

Obinutuzumab is a medicine that may help destroy abnormal (cancerous) B cells. Obinutuzumab is a type of antibody. Antibodies are normally made by the body's immune system to fight off infections and keep you healthy, but they can also be made in a laboratory to treat a variety of diseases, including FL. Obinutuzumab attaches itself to a protein called CD20 that is found on the surface of lymphoma (abnormal, cancerous B cells) and normal B cells.

A standard treatment for lymphoma includes combining antibody medicines with other medicines that treat cancer, called chemotherapy medicines. Obinutuzumab is given to patients by an infusion into the vein (called an intravenous infusion) over 3–4 hours. In this study, researchers wanted to see if it is safe to infuse the same amount of obinutuzumab in 90 minutes instead of 3–4 hours. The side effects were looked at,

especially during the infusion or in the 24 hours after the infusion. Shortening the infusion time is expected to make treatment easier for patients and faster for clinics.

## What is the medicine being studied?

This study looked at 1 medicine:

- **Obinutuzumab** – the medicine that was studied.

'Obinutuzumab' is the medicine that was studied here – researchers looked at whether it is safe to give obinutuzumab to patients by infusion into the vein (called intravenous infusion) faster than they currently give it (in approximately 90 minutes instead of the standard 3-4 hours)

- You say this as 'oh-bi-nue-tooz-ue-mab'.
- Obinutuzumab is an antibody medicine that may help destroy lymphoma (cancerous B cells).

## What do researchers want to find out?

- Researchers did this study to find out if it is safe to infuse obinutuzumab faster into patients' veins, by checking how many people had reactions considered specifically related to the faster infusion during or following the infusion (infusion related reactions) and seeing how serious they were (see section 4: 'What were the results of the study?').

**The main question that researchers wanted to answer is:**
How many patients get potentially serious reactions from having a faster infusion of obinutuzumab? Researchers looked at all possible side effects, but they specifically focused on side effects that happen during the infusion or in the 24 hours after the infusion (so-called "infusion-related reactions").

## What kind of study is this?

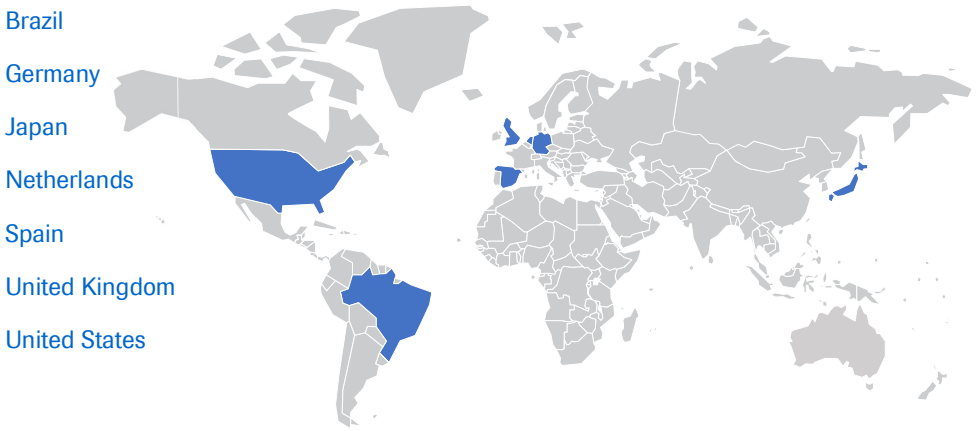
This study is a 'Phase 4' study. This means that the study was done after obinutuzumab had been approved for doctors to give to patients. In this study, obinutuzumab was given in a different way. It was given (infused) in about 90 minutes instead of the standard 3-4 hours.

This was an 'open label' study. This means that both the people taking part in the study and the study doctors knew which of the study medicines people were taking.

## When and where is the study taking place?

The study started in February 2019. This summary includes the final results that were collected and analysed by April 2023. At the time of writing this summary, the study has been completed – patients are no longer treated in this study and study doctors are no longer collecting information.

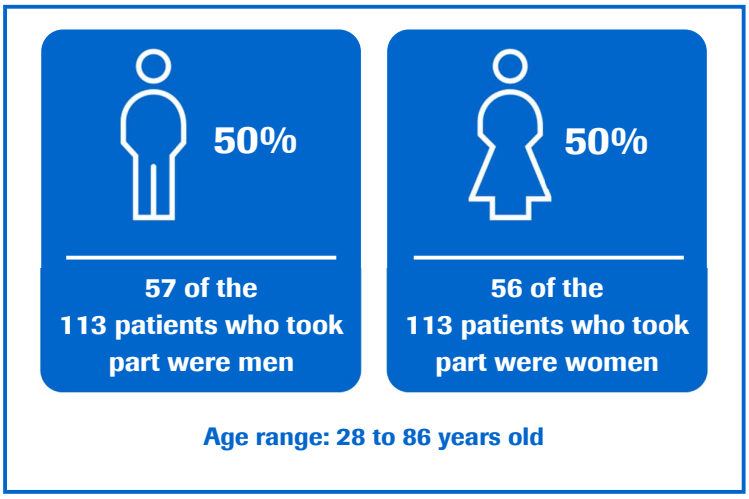
The study took place at 32 study centres – across 7 countries in North America, South America, and Europe. The following map shows the countries where this study took place.




## 2. Who is taking part in this study?

In this study, 113 people with a certain type of cancer of the lymphatic system called follicular lymphoma took part.

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




People could take part in the study if:

- If they were 18 years or older
- If they had untreated advanced FL
- If they had the CD20 protein

People could not take part in the study if:

- If they already had treatment for FL before but the treatment did not work or the cancer came back
- If they had been given any treatment for FL before
- If they had been taking certain medications

## 3. What happened during the study?

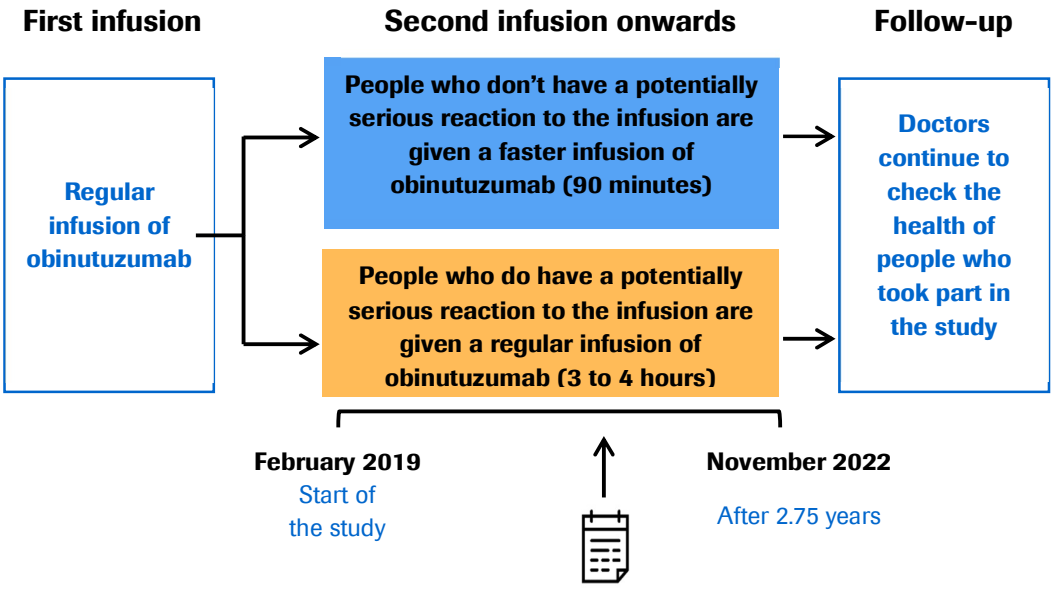
The study is divided into two phases. In the first phase, people were given obinutuzumab along with a standard chemotherapy for 6 to 8 cycles, depending on the chemotherapy medicines. Then in the second phase, people were given obinutuzumab by itself every 8 weeks for 12 cycles (up to 2 years), or until their cancer got worse.

The treatment being looked at was:

- **Obinutuzumab** (the medicine being studied) – it was given by infusion into the vein (intravenous infusion) every 8 weeks.

- The first time people were given obinutuzumab, it was infused into their vein over the regular amount of time, which is about 3 to 4 hours.
- If people did not have a potentially serious reaction to the infusion, obinutuzumab was infused faster the next time they had it, in about 90 minutes (1 and a half hours).
- People kept getting the faster infusion every time they went to the clinic.
- If people had a potentially serious reaction from the faster infusion, they were switched back to the regular infusion.

This study is still happening so doctors still check the health of people who took part in the study. Look below to see more information about what has happened in the study so far – and what the next steps are.

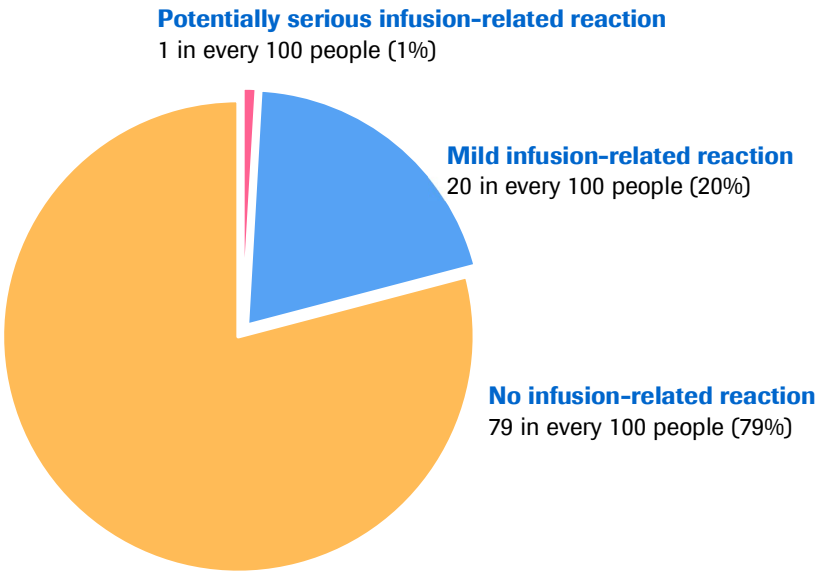


This study is still happening, so the symbol on the timeline (📋) shows when the information shown in this summary was collected – after 21 months (December 2020).

## 4. What were the results of the study?

Researchers specifically focused on potentially serious reactions that appear during or in the next 24 hours of the infusion (so-called "infusion-related reactions"). Of the 113 patients who took part in the study, 110 patients received the faster (short) infusion. 1 out of 110 people given the faster infusion of obinutuzumab had a potentially serious infusion-related reaction to the infusion. 22 out of the 110 people given the faster infusion of obinutuzumab had a mild infusion-related reaction to the infusion, mostly feeling sick (nausea) and throwing up.

**On average, 1 in 100 people have a potentially serious reaction that happened during the infusion (drip into a vein) of obinutuzumab, or in the next 24 hours after the infusion (so-called "infusion-related reactions").**




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.

This section explains all side effects seen with the infusion of obinutuzumab, including infusion-related reactions (side effects that happened during the infusion or in the next 24 hours after the infusion), as well as side effects that can appear weeks or months after the infusion.

- Side effects may or may not be related to the treatment 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.

Around 99 in 100 patients (99%) in the study had at least one side effect that may or may not have been related to obinutuzumab.

Around 90 in 100 patients (90%) in the study had at least one side effect of any intensity (meaning it could have been serious or not serious) that was considered by the doctor to be related to obinutuzumab.

### Serious side effects

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

During the first part of this study, obinutuzumab was given with chemotherapy medicines. During this study, around 40out of every 100 people (40%) had at least one serious side effect that may or may not have been related to obinutuzumab.

The most common serious side effects are shown in the following table – these are the 3 most common serious side effects in people treated with obinutuzumab. 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** | **People taking obinutuzumab** (113 people total) |
|---|---|
| COVID-19 | 5% (6 out of 113) |
| COVID-19 lung infection (pneumonia) | 6% 7 out of 113 |
| Lung infection (pneumonia) | 5% (6 out of 113) |
| Fever associated with dangerously low levels of a type of white blood cell (neutrophils) | 5% (6 out of 113) |
| Low level of white blood cells | 3% (3 out of 113) |

Nine out of 113 people died during the study. Two patients died from the cancer, one patient died from cardiac arrest, and six patients died from infections or infection-related complications. Of the 9 deaths, 2 deaths were related to study treatment.
During the study, some people decided to stop taking their medicine because of side effects:

- 15 out of 113 people (13%) stopped taking their medicine because of side effects.

## Most common side effects

- During this study, 99 out of every 100 people (99%) had a side effect that may or may not have been related to taking obinutuzumab.

The 8 most common side effects seen in people who took part in the study are shown in the following table. Some people had more than one side effect, which means that they can be counted in more than one row.

| **Most common side effects reported in this study** | **People taking obinutuzumab** (113 people total) |
|---|---|
| Low level of white blood cells | 64% (72 out of 113) |
| Reactions to the infusion (drip into the vein) | 62% (70 out of 113) |
| Feeling sick (nausea) | 43% (49 out of 113) |
| Constipation | 36% (41 out of 113) |
| Low level of a type of white blood cells called lymphocytes | 20% (23 out of 113) |
| Difficulty falling asleep at night (insomnia) | 20% (24 out of 113) |
| Pyrexia | 20% (23 out of 113) |
| Headache | 20% (23 out of 113) |

Another piece of information that researchers collected was the types of reactions patients get from faster infusion of obinutuzumab.

- The most common reactions after a faster infusion of obinutuzumab were:
  - Feeling sick (nausea)
  - throwing up
  - not feeling hungry

## 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 113 people with cancer of the lymph nodes – called follicular lymphoma. These results helped researchers learn more about using obinutuzumab in treating cancer of the lymph nodes.

Patients from 32 study centres across 7 countries participated in this study.

In this study, researchers wanted to find out if it was safe to infuse obinutuzumab faster into patient's veins when they were being treated for FL. Looking at infusion-related reactions (side effects that happened during the infusion or 24 hours after the infusion), the study showed that 1 in 100 people had a serious infusion-related reaction from a faster intravenous infusion (drip into a vein) of obinutuzumab. About 20 in 100 people had a mild to moderate infusion-related reaction to the faster infusion, and 79 in 100 people had no infusion-related reaction from having a faster infusion of obinutuzumab. The most common side effects after a faster infusion of obinutuzumab were feeling sick (nausea), throwing up, and not feeling hungry.

Looking at all possible side effects, even weeks or months after the infusion of obinutuzumab, the most common side effects (that may or may not have been related to taking obinutuzumab) in this study were low levels of different types of blood cells, reactions to the infusion, feeling sick (nausea) and difficulty falling asleep at night (insomnia). The most serious side effects in this study were lung infection (pneumonia), fever associated with low levels of white blood cells and low levels of white blood cells.

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 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.

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## 7. Are there plans for other studies?

Studies with obinutuzumab are still happening. Further studies may be planned depending on potential future scientific/medical questions.

## 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/NCT03817853
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2018-003255-38/results
- https://forpatients.roche.com/en/trials/cancer/non-hodgkins-lymphoma/an-open-label--single-arm-study-of-obinutuzumab-short-d-96747.html

If you would like to find out more about the results of this study, the full title of the relevant conference abstract is: “Obinutuzumab short-duration infusion (SDI) in previously untreated advanced follicular lymphoma: Results from the end of induction analysis of the phase IV GAZELLE study.” The authors of the scientific paper are: Miguel Angel A. Canales Albendea, Thomas A. Buchholz, Koji Izutsu, Takayuki Ishikawa, Laura Maria Fogliatto, and others. The abstract is published in the journal ‘Journal of Clinical Oncology’, volume number 39, on pages 7545-7545.

## 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/non-hodgkins-lymphoma/an-open-label--single-arm-study-of-obinutuzumab-short-d-96747.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 multicentric, open-label, single arm study of obinutuzumab short duration infusion (SDI) in patients with previously untreated advanced follicular lyphoma”.

The study is known as ‘GAZELLE’.

- The protocol number for this study is: MO40597.
- The ClinicalTrials.gov identifier for this study is: NCT03817853.
- The EudraCT number for this study is: 2018-003255-38.