Summary of Clinical Trial

A study to investigate how well glofitamab works in people with a type of blood cancer called 'B-cell non-Hodgkin's lymphoma'.

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 general 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 2017. This summary includes the results that were analysed in June 2022. At the time of writing this summary, the study is ongoing – study doctors are still collecting information. This summary will be updated when the study ends.

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

Glossary

- **Non-Hodgkin's Lymphoma (NHL) =** a cancer of the lymph nodes.
- **Diffuse large B-cell lymphoma (DLBCL)** = a fast-growing cancer of the lymph nodes. It is the most common type of lymphoma.
- **Relapsed or refractory** = the cancer has come back after being treated

or did not get better with the previous treatment.

Thank you to the people who took part in this study

The people who took part in this study have helped researchers to answer important questions about types of non-Hodgkin's lymphoma (NHL) and the medicine studied – 'glofitamab'. The types of non-Hodgkin's lymphoma that were studied included:

- Diffuse large B-cell lymphoma (DLBCL)
- Large B-cell Lymphoma transformed from follicular lymphoma (TFL)
- High Grade large B-cell Lymphoma (HGBCL)
- Primary mediastinal B-cell lymphoma (PMBCL)

1. General information about this study

Why was this study done?

Non-Hodgkin's lymphoma (NHL) is a type of cancer that occurs when white blood cells grow abnormally and form tumours throughout the body. It is one of the leading causes of cancer death in both the United States and Europe. Most NHL cases happen in the B-cells, which are a type of white blood cell. There are different types of B-cell NHLs, such as DLBCL. People with NHL may be given several different types of treatment, including:

- **Chemotherapy** – medicines that use chemicals to kill cancer cells in the body.
- **Immunotherapy** – medicines that stimulate the body's immune system to kill cancer cells.
- **Bone marrow transplant** - a procedure where healthy stem cells that produce blood are infused into the body to replace unhealthy or damaged bone marrow.

Despite recent treatment advances, NHL can return after successful treatment (known as relapsed NHL) or may not respond to treatment (known as refractory NHL). There is a need for new treatment options to improve outcomes for patients with NHL.

People in this study had previously been given two or more treatments for NHL, but these did not work (refractory NHL), or the cancer came back after treatment (relapsed NHL).

This study looked to see whether glofitamab worked, and was safe, for people with relapsed or refractory NHL.

What was the medicine being studied?

This study involved two medicines.

'**Glofitamab'** is the main medicine investigated in this study.

- You say this as 'glow – fit – ah – mab'.
- Glofitamab is a new antibody (a type of immunotherapy). Antibodies are proteins normally produced by the body's immune system that bind (stick) to bacteria and viruses to help the body destroy them. Some antibodies, like glofitamab, are made in the laboratory to detect bad cells such as cancer and help destroy them. Glofitamab binds two targets. One target is a specific protein called CD20 on the surface of cancerous B-cells. The other target is a protein complex called CD3 on the surface of T-cells, which are a type of white blood cell that is important in the body's immune system.
- By binding T-cells near the cancerous B-cells, the medicine acts like a bridge to bring the cancer cells and T-cells together. This encourages the T-cells to destroy the cancer cells and helps control the disease.

'**Obinutuzumab'** is the other medicine used in this study.

- You say this as 'oh – bin – oo – too – zoo – mab'.
- Obinutuzumab is also an antibody (a type of immunotherapy) that binds to the CD20 protein on the surface of B-cells. Obinutuzumab is expected to reduce the risk of side effects from glofitamab treatment.

What did researchers want to find out?

Researchers did this study to find out how well glofitamab worked in people with relapsed or refractory NHL. This was done by seeing how many people had no cancer left after treatment with glofitamab. They also wanted to find out how safe glofitamab was in these people. This was done by seeing how many people had side effects and how serious they were, when taking glofitamab (see section 5 "What were the side effects?").

The main questions that researchers wanted to answer were:

1. Does glofitamab work in people with relapsed or refractory NHL?
2. Is glofitamab safe in people with relapsed or refractory NHL?

What kind of study was this?

This study was a 'Phase 1/2' study. This was the first study for glofitamab for people with NHL. People with NHL took a single dose of obinutuzumab before starting glofitamab, to find out about the safety of these medicines and whether they worked to make the cancer smaller or go away completely.

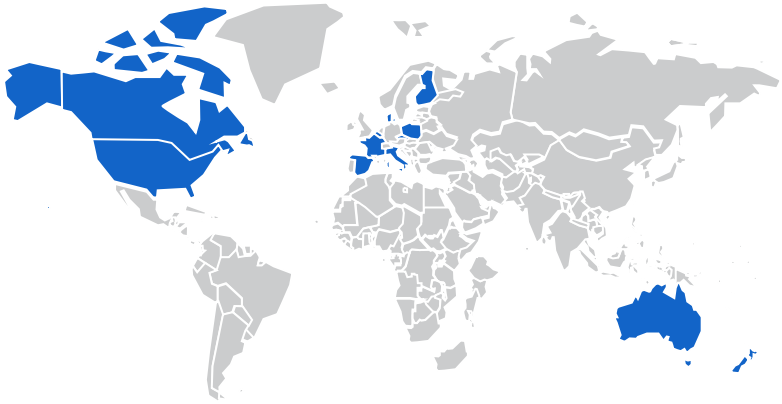
This was an 'open-label' study. This means that both the people taking part in the study and the study doctors knew what amount of glofitamab people were taking.

When and where did the study take place?

The study started in February 2017. This summary includes the results up until June 2022. At the time of writing this summary, the study was ongoing – study doctors are still collecting information.

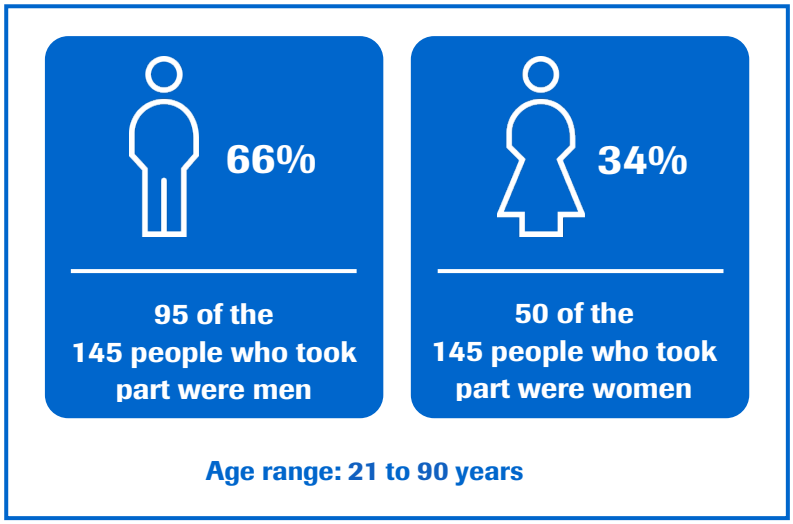
The study took place at 41 study centres - across 13 countries in Europe, North America, East Asia and Oceania. The following map shows the countries where this study took place.

Australia
Belgium
Canada
Czech Republic
Denmark
Finland
France
Italy
New Zealand
Poland
Spain
Taiwan
United States



2. Who took part in this study?

This summary includes the results that were analysed in June 2022. In this study, 145 people with NHL who took part. More information on the people who took part is given below.



People could take part in the study if they:

- had received at least two previous treatments for their cancer, but the treatments did not work (refractory NHL), or the cancer came back after each treatment (relapsed NHL)
- were over 18 years old
- had no other available treatment options that were expected to prolong survival
- had disease that could be measured by the size of the lymph nodes
- had functioning liver, kidney, and blood systems

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

- had a severe infection
- had a disease of the heart and blood vessels
- had recently had
    - certain medicines that affect the immune system
    - radiotherapy, chemotherapy, or other anti-cancer agents
    - bone marrow transplant
- had certain illnesses where the immune system attacks the body (autoimmune disease)
- had another cancer within 2 years of the study (except very low risk cancers, that are not likely to come back)

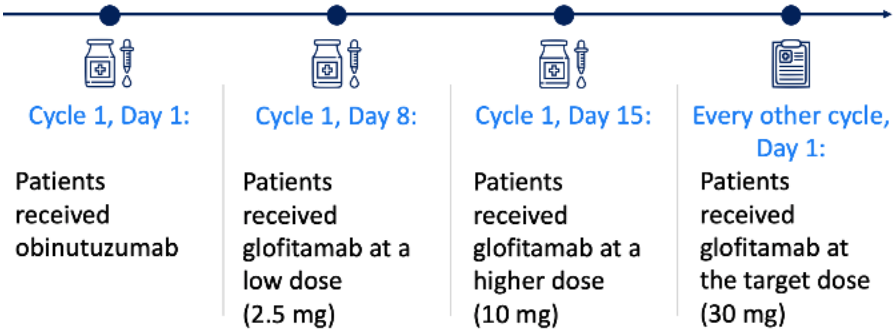
3. What happened during the study?

During the study, people received glofitamab at different doses. One week before receiving the first dose of glofitamab, patients received one dose of obinutuzumab. Obinutuzumab was given with the intention to reduce the risk of certain side effects.

All people received treatment with glofitamab after one dose of obinutuzumab, and were also pre-treated with a steroid, analgesic, and an antihistamine.

All treatments were given by drip (infusion) into a vein.

The medicines in this study were given in 'treatment cycles.' Each treatment cycle lasted 3 weeks.



One hour before each obinutuzumab and glofitamab treatment, most people had steroid treatment with methylprednisolone, prednisone, or dexamethasone. A sub-group of people received only dexamethasone, which is a specific type of steroid that has a longer activity than the other steroids.

This study is ongoing, so some people are still being treated with the study medicines. When the study finishes, people who had no cancer left after their treatment with glofitamab will be asked to go back to their study centre, to see if they are still free of cancer. Look below to see more information about what has happened in the study so far – and what the next steps are.

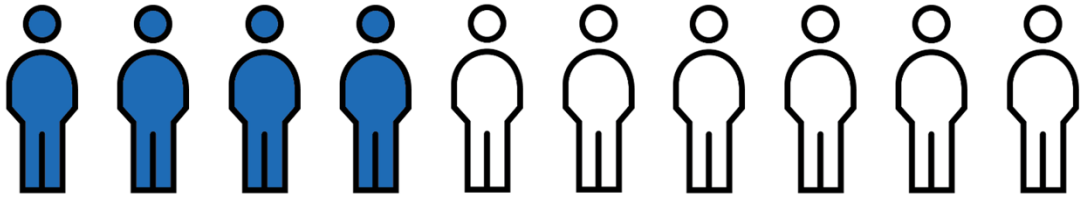
4. What were the results of the study?

Question 1: Does glofitamab work in people with relapsed or refractory B-cell NHL?

Out of the 145 total patients, researchers looked at a group of 132 patients with two specific types of NHL, DLBCL and TFL , to see if glofitamab worked. They did this by looking at how many of these 132 people had no cancer left following treatment with glofitamab.

There is more information about the types of NHL seen in this study at the start of this summary.

- Overall, 57 out of 132 people (43%) had no cancer left after having glofitamab treatment.
- At the time of this study, half of the people who received glofitamab were free of their cancer for over 18.4 months. Half of the people were free of their cancer for less than this.



Around 4 in every 10 people (43%) had no cancer left after receiving glofitamab

Question 2: Is glofitamab safe in people with relapsed or refractory B-cell NHL?
Researchers asked the 145 people in the study about any side effects – such as nausea or the urge to vomit – that happened during the study. People in the study also had regular tests to measure their heart activity, breathing, weight, body temperature, and blood pressure.

- 48% of people had a serious side effect related to glofitamab treatment.
- Only 7% of the 145 people stopped taking glofitamab due to side effects.

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 fever) 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 severe and can vary 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, 48% of the 145 people in the study had at least one serious side effect. The most common serious side effects were:

- Aggressive immune system response (cytokine release syndrome)
- COVID-19 infection
- Shock caused by infection (sepsis)
- Swelling and inflammation of the lymph nodes (tumour flare)

Common means that at least 2 in 100 people in the study experienced these side effects. Some people had more than one side effect.

In the study, 5% of people died due to side effects that may have been related to one of the study medicines. These are shown in the following table.

Fatal side effects reported in this study	**People in the study** (145 total)
COVID-19 infection	3.4%
Shock caused by infection (sepsis)	1.4%
Sudden change in thinking or behaviour (delirium)	0.6%

During the study, 7% of people decided to stop taking their medicine because of side effects, such as:

- Infection
- A decrease in the number of a type of white blood cell (neutropenia)
- Sudden change in thinking or behaviour (delirium)
- Aggressive immune system response (cytokine release syndrome)

Most common side effects

Of the 145 people, 99% experienced at least one side effect.

The most common side effects are shown in the following table – these are the four most common side effects. Some people had more than one side effect – this means that they are included in more than one row in the table.

Common side effects reported in this study	**People affected in the study** (145 total)
Aggressive immune system response (cytokine release syndrome)	70%
Muscle and bone pain (musculoskeletal pain)	21%
Rash	20%
Fatigue	20%

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 154 people with relapsed or refractory DLBCL These results helped researchers learn more about glofitamab and DLBCL.

This study looked at whether glofitamab worked and was safe in people with relapsed or refractory B-cell DLBCL, following pre-treatment with obinutuzumab.

Overall, 57 out of 132 (43%) people who at least one dose of glofitamab had no cancer left.

Serious side effects were reported in 48% out of 145 people. Of the 145 people who had treatment with glofitamab, 7% stopped taking the glofitamab due to side effects.

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?

Studies with glofitamab as a treatment on its own, and in combination with other therapies, are ongoing, and further studies are planned.

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/NCT03075696
- https://forpatients.roche.com/en/trials/cancer/non-hodgkins-lymphoma/a-dose-escalation-study-of-ro7082859-as-a-single-agent-and-in-co.html

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: "**Glofitamab for Relapsed or Refractory Diffuse Large B-Cell Lymphoma".** The authors of the scientific paper are: Michael J Dickinson, Carmelo Carlo-Stella, Franck Morschhauser, Guillaume Cartron, and others. The paper is published in the 'New England Journal of Medicine', volume number 387, on pages 2220-2231.

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/a-dose-escalation-study-of-ro7082859-as-a-single-agent-and-in-co.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 Multicenter, Open-Label, Phase I/II Study to Evaluate the Safety, Efficacy, Tolerability and Pharmacokinetics of Escalating Doses of Glofitamab (RO7082859) as a Single Agent and in Combination With Obinutuzumab Administered After a Fixed, Single Dose Pre-Treatment of Obinutuzumab (Gazyva®/Gazyvaro™) in Patients With Relapsed/Refractory B-Cell Non-Hodgkin's Lymphoma”.

- The protocol number for this study is: NP30179.
- The ClinicalTrials.gov identifier for this study is: NCT03075696.