

## Summary of Clinical Trial Results

### A study of obinutuzumab with chemotherapy in comparison with rituximab with chemotherapy in patients with non-Hodgkin's 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
- patients who took part in the study.

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

The study started in July 2011 and finished in July 2021. 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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#### Glossary

- NHL = cancer of the lymphatic system called 'non-Hodgkin's lymphoma'
- Follicular lymphoma = the most common type of NHL.

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

The patients who took part have helped researchers to answer important questions about a cancer of the lymphatic system called 'non-Hodgkin's lymphoma' or 'NHL', 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 non-Hodgkin's lymphoma, or NHL. Most patients in this study had a type of NHL called "follicular lymphoma".
- In this study, patients were given either the medicine being studied (called 'obinutuzumab') or an existing medicine (called 'rituximab'), both in combination with chemotherapy – it was decided by chance which treatment each person was given.
- This study included 1401 patients at 177 study centres across 18 countries. 1202 of these patients had follicular lymphoma.
- The main finding was that fewer patients in the obinutuzumab group had their cancer get worse compared to patients in the rituximab group. A total of 206 of 601 (34%) patients with follicular lymphoma had their cancer get worse in the obinutuzumab group compared to 244 of 601 patients (41%) with follicular lymphoma in the rituximab group.
- Around 49% of patients with follicular lymphoma (291 out of 595 patients) taking obinutuzumab had serious side effects (which may or may not have been related to the study drug administered), compared to around 43% of patients (259 out of 597 patients) taking rituximab.

## 1. General information about this study

### Why was this study done?

Researchers were looking for a different way to treat a certain type of cancer of the lymphatic system called non-Hodgkin's lymphoma, or NHL. The lymphatic system is an important part of the immune system (it includes, for example, the lymph nodes and the spleen). People with NHL have higher levels of abnormal B cells in their body. B cells are a type of white blood cells. The most common type of NHL is follicular lymphoma. Most of the patients in the study had follicular lymphoma that had not been treated yet, but some people had a different kind of NHL called marginal zone lymphoma, or MZL.

Obinutuzumab is a drug 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 NHL. 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 drugs. In this study, researchers wanted to compare how well obinutuzumab worked to treat cancer compared to a drug called rituximab, when these two drugs were combined with a standard chemotherapy. Rituximab is another antibody medicine that targets CD20 and is often considered routine care for this type of disease.

This study enrolled men and women who were at least 18 years old. All of them had advanced stages of certain types of NHL, most of them a type called follicular lymphoma, and had tumours that had CD20.

## What were the study medicines?

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This study looked at 2 medicines:

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

‘Rituximab’ is an existing medicine given to people with NHL in combination with chemotherapy drugs. You say this as ‘ruh-tuhk-suh-mab’.

- Rituximab is an antibody drug that may help destroy lymphoma (cancerous B cells).

‘Obinutuzumab’ is the medicine that was studied here – it works in a similar way to rituximab, but there are some differences in the strength and the way it works.

- You say this as ‘oh-bi-nue-too-ue-mab’.
- Obinutuzumab is an antibody drug that may help destroy lymphoma (cancerous B cells).
- Obinutuzumab is similar to rituximab but might work better.

## What did researchers want to find out?

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- Researchers did this study to compare obinutuzumab with rituximab (both given in combination with a standard chemotherapy) to see how well obinutuzumab worked (see section 4 “What were the results of the study?”).
- They also wanted to find out how safe the medicine was by checking how many patients had side effects and seeing how serious they were, when taking each of the medicines during this study (see section 5 “What were the side effects?”).

### **The main question that researchers wanted to answer was:**

1. Did fewer patients who received obinutuzumab with chemotherapy have their cancer get worse compared to patients who received rituximab with chemotherapy?

### **Other questions that researchers wanted to answer included:**

2. Did patients who received obinutuzumab with chemotherapy live longer compared to patients who received rituximab with chemotherapy?
3. Did fewer patients who received obinutuzumab with chemotherapy have to start a new or different treatment for their cancer compared to patients who received rituximab with chemotherapy?
4. How did the study treatments affect patients’ quality of life?
5. What side effects did patients have from the study treatments?

## What kind of study was this?

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This study was a ‘Phase 3’ study. This means that obinutuzumab had been tested in a smaller number of people with NHL before this study. In this study, a larger number of people with NHL either took obinutuzumab or rituximab (the standard treatment for NHL) in combination with a standard chemotherapy.

The study was 'randomised'. This means that it was decided by chance which of the medicines people in the study would have – like tossing a coin. Randomly choosing which medicine people take makes it more likely that the types of people in both groups (for example, age, race) will be a similar mix. Apart from the exact medicines being tested in each group, all other aspects of care were the same between the groups.

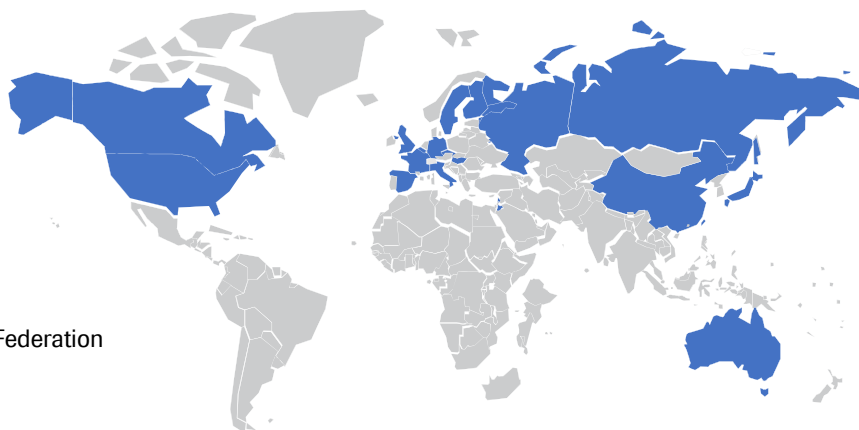
This was an 'open label' study. This means that both the people taking part in the study and the study doctors knew which of the study medicines people were given.

## When and where did the study take place?

The study started in July 2011 and finished in July 2021. This summary was written after the study had ended.

The study took place at 177 study centres – across 18 countries in North America, Australia, Europe, and Asia. The following map shows the countries where this study took place.

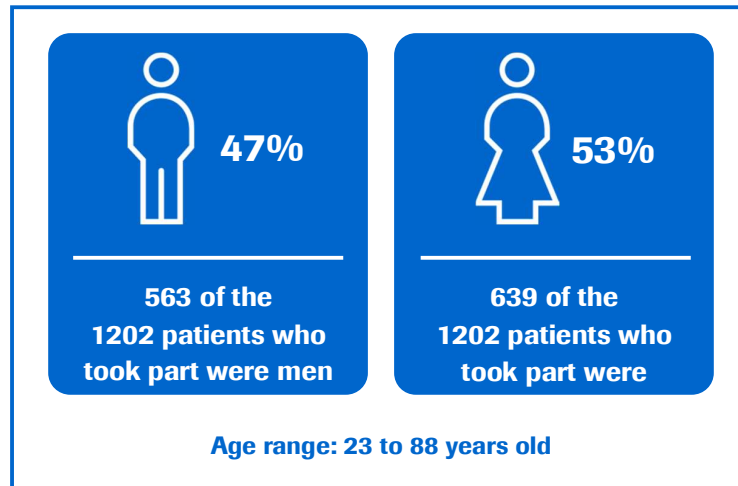
- Australia
- Belgium
- Canada
- China
- Czechia
- Finland
- France
- Germany
- Hungary
- Israel
- Italy
- Japan
- Russian Federation
- Spain
- Sweden
- Taiwan
- United Kingdom
- United States of America



## 2. Who took part in this study?

In this study, 1401 patients with NHL took part. Of the patients in the study, 1202 patients had the type of NHL called "follicular lymphoma". In this summary we describe the patients with follicular lymphoma.

patients who took part in the study were between 23 and 88 years of age. 563 of the 1202 patients (47%) were male and 639 of the 1202 patients (53%) were female. The average age of patients who took part was 58 years old. More information on the patients who took part is given below.



Patients could take part in the study:

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

Patients could not take part in the study:

- If they had other types of lymphoma
- If they had a history of severe allergic reactions to the types of drugs being tested

### 3. What happened during the study?

During the study, patients were selected by chance to get one of two treatments. The treatments were selected at random – by a computer.

The treatment groups were:

- **Obinutuzumab** (the medicine being studied) – infused into a vein over a certain time span (called IV infusion). Details of how often the dose was given are below.
- **Rituximab** (existing medicine) – injected into a vein (IV infusion). Details of how often the dose was given are below.

In both groups, patients received a standard chemotherapy together with obinutuzumab or rituximab.

Before the study began, the person’s doctor selected one of three chemotherapies (all are standard chemotherapies) that was given together with the antibody treatment:

- Either CHOP (a combination of cyclophosphamide, doxorubicin, vincristine, and prednisone),
- Or CVP (a combination of cyclophosphamide, vincristine, and prednisone),
- Or bendamustine

**Part 1 of the treatment lasted about 6-8 months and was called the “Induction Period”.**

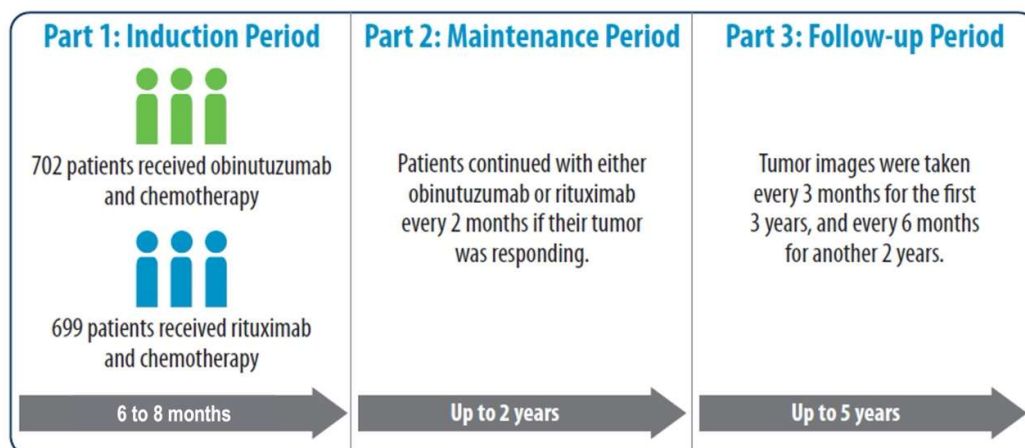
During Part 1, patients received chemotherapy and either obinutuzumab or rituximab. Patients received obinutuzumab or rituximab as an intravenous infusion (which means the treatment was infused into a vein using over a certain time span). The chemotherapy treatments were given by mouth (orally) or intravenously, depending on the type of chemotherapy.

Study doctors regularly took images of tumours to see if and how they were responding to the treatments.

**Part 2 lasted up to 2 years and was called the “Maintenance Period”.** After patients finished Part 1 of the study, study doctors checked how their cancer responded to the treatment. Patients could move on to Part 2 if their tumour shrunk by at least 50% of its original size or even fully disappeared for a time. Patients who entered Part 2 received only obinutuzumab or rituximab every 2 months for up to 2 years, without any chemotherapy drugs.

**Part 3 was called the “Follow-up Period”.** Patients were asked to return to the clinic every 3 months for the first 3 years and then every 6 months for another 2 years. During this part of the study, doctors took images of tumours to see how they were responding to the treatments and if the response lasted after end of treatment, performed examinations, and asked how the person was feeling.

The figure below shows what happened during each part of the study.



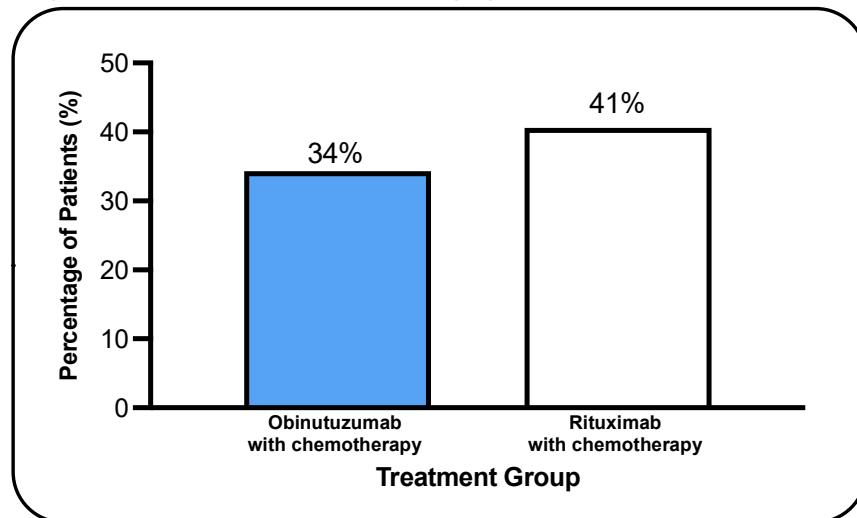
## 4. What were the results of the study?

### Question 1: Did fewer patients who received obinutuzumab with chemotherapy have their cancer get worse compared to patients who received rituximab with chemotherapy?

Researchers looked at how much time there was between the start of the study and patients' cancer getting worse. Fewer patients who received obinutuzumab with chemotherapy had their cancer get worse or compared with patients who received rituximab. In this study, "get worse" meant that additional tumours appeared, tumours increased in size, or patients died for any reason.

Researchers looked at the effect of the treatments on patients with follicular lymphoma. A total of 206 of 601 patients (34%) had their cancer get worse in the obinutuzumab group compared to 244 of 601 patients (41%) in the rituximab group. The graph below shows these results for patients with follicular lymphoma in the study.

Proportion of Patients with Follicular Lymphoma Whose Cancer Got Worse



### Question 2: Did patients who received obinutuzumab with chemotherapy live longer compared to patients who received rituximab with chemotherapy?

Another piece of information that researchers collected was how many patients were alive at the end of the study. For patients with follicular lymphoma:

- 525 of 601 (87%) of patients in the obinutuzumab group were alive
- 515 of 601 (86%) of patients in the rituximab group were alive.

### Question 3: Did fewer patients who received obinutuzumab have to start a new or different treatment for their cancer compared to patients who received rituximab?

If patients with follicular lymphoma had tumours that got worse, they may have had to start a new or different treatment for their cancer. Researchers found that fewer patients in the obinutuzumab group had to start a different treatment for their lymphoma compared to patients in the rituximab group. For patients with follicular lymphoma:

- 119 of 601 (20%) of patients in the obinutuzumab group had to start a different treatment.
- 176 of 601 (29%) of patients in the rituximab group had to start a different treatment.

#### **Question 4: How did the study treatments affect patients' quality of life?**

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Researchers used two different questionnaires to ask patients how their quality of life was after treatment. The surveys looked at patients' physical, social, emotional, and functional well-being. They also asked questions about how severe patients' lymphoma-related symptoms were. Overall, researchers found no difference between the two treatment groups in patients' quality of life.

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 (reported adverse events) are medical problems (such as feeling dizzy) that happen during the study that may or may not be related to the study drug administered.

- Not all of the patients in this study had all of the side effects.
- Side effects may be mild to very severe any 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**

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

During this study, about 1 in every 2 patients with follicular lymphoma (46%) had at least one serious side effect. Around 49% of patients taking obinutuzumab had a serious side effect, compared with around 43% of patients taking rituximab.

The most common serious side effects for patients with follicular lymphoma are shown in the following table – these are the 6 most common serious side effects across both treatment groups. Some patients had more than one side effect – this means that they are included in more than one row in the table.



<b>Serious side effects reported in this study</b>	<b>Patients taking obinutuzumab (595 patients total)</b>	<b>Patients taking rituximab (597 patients total)</b>
Lung infection (pneumonia)	6% (35 out of 595)	6% (37 out of 597)
Low levels of neutrophils, a type of white blood cell that fights infection	4% (24 out of 595)	5% (28 out of 597)
Low white blood cell levels with fever due to infection	5% (31 out of 595)	3% (18 out of 597)
An immune system reaction to the study medicine being given by a drip into the vein (infusion-related reaction)	5% (27 out of 595)	2% (12 out of 597)
Fever	3% (18 out of 595)	3% (16 out of 597)
Shingles (a painful, blistering rash in one part of the body)	1% (8 out of 595)	1% (8 out of 597)

There were some patients in the study who died due to side effects that may or may not have been related to one of the study medicines. These were:

- 26 out of 595 patients (4%) in the obinutuzumab group.
- 27 out of 597 patients (5%) in the rituximab group.

During the study, some patients decided to stop taking their medicine because of side effects (that may or may not have been related to the study medicines):

- In the obinutuzumab group, 98 out of 595 patients (16%) stopped taking their medicine.
- In the rituximab group, 88 out of 597 patients (15%) stopped taking their medicine.

### **Most common side effects**

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During this study, more than 99 out of 100 patients had a side effect that was not considered serious. More than 99 out of 100 patients taking obinutuzumab had a side effect that was not considered serious, and so did more than 99 out of 100 patients taking rituximab.

The most common side effects for patients with follicular lymphoma are shown in the following table – these are the 7 most common side effects across both treatment groups. Some patients had more than one side effect – this means that they are included in more than one row in the table.

<b>Most common side effects reported in this study</b>	<b>Patients taking obinutuzumab</b> (595 patients total)	<b>Patients taking rituximab</b> (597 patients total)
An immune system reaction to the study medicine being given by a drip into the vein (infusion-related reaction)	61% (363 out of 595)	51% (303 out of 597)
Low levels of neutrophils, a type of white blood cell that fights infection	51% (305 out of 595)	47% (279 out of 597)
Nausea	50% (270 out of 595)	50% (259 out of 597)
Constipation	37% (217 out of 595)	34% (200 out of 597)
Vomiting	26% (157 out of 595)	23% (135 out of 597)
Chills	17% (103 out of 595)	10% (59 out of 597)
Hair loss	13% (78 out of 595)	11% (66 out of 597)

### 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.

Ten side effects were of particular interest in the study because scientists knew that they could have been caused by the study drugs. 5 of these 10 side effects happened more in patients taking obinutuzumab than those taking rituximab. These side effects were reactions from the drug being injected, infection, low blood platelet counts, heart issues, and developing a new cancer.

## 6. How has this study helped research?

The information presented here is from a single study of 1401 people with NHL. Most people in the study (1202) had a type of NHL called follicular lymphoma. These results helped researchers learn more about follicular lymphoma and obinutuzumab.

Patients from 177 study centres across 18 countries participated in this study.

In this study, researchers compared obinutuzumab with chemotherapy to rituximab with chemotherapy in people with different types of NHL, mostly follicular lymphoma. They found that fewer patients who received obinutuzumab with chemotherapy had their cancer get worse compared to patients who received rituximab with chemotherapy. They also found that fewer patients who received obinutuzumab had to start a new or different treatment for their cancer compared to patients who received rituximab.

The proportion of patients alive at the end of the study was similar in both groups, and there was no difference between the two treatment groups in patients' quality of life.

In both groups, most patients had at least one side effect. The safety of obinutuzumab and rituximab was similar.

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 obinutuzumab are still happening, and 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/NCT01332968>
- <https://www.clinicaltrialsregister.eu/ctr-search/trial/2010-024132-41/results>
- <https://forpatients.roche.com/en/trials/cancer/non-hodgkins-lymphoma/a-study-in-patients-with-nhl.html>

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: “Immunochemotherapy with Obinutuzumab or Rituximab for Previously Untreated Follicular Lymphoma in the GALLIUM Study: Influence of Chemotherapy on Efficacy and Safety”. The authors of the scientific paper are: Wolfgang Hiddemann, Anna Maria Barbui, Miguel A Canales, Paul K Cannell, Graham P Collins, and others. The paper is published in the journal ‘Journal of Clinical Oncology’, volume number 36, no. 23 (published August 10, 2018), on pages 2395-2404.

## **Who can I contact if I have questions about this study?**

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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-study-in-patients-with-nhl.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?**

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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**

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The full title of this study is: “A Multicenter, Phase III, Open-Label, Randomized Study in Previously Untreated Patients with Advanced Indolent Non-Hodgkin’s Lymphoma Evaluating the Benefit of GA101 (RO5072759) plus Chemotherapy Compared with Rituximab plus Chemotherapy Followed by GA101 or Rituximab Maintenance Therapy in Responders”.

The study is known as ‘GALLIUM’.

- The protocol number for this study is: BO21223.
- The ClinicalTrials.gov identifier for this study is: NCT01332968.
- The EudraCT number for this study is: 2010-024132-41.