

# Clinical Trial RESULTS

**Research Sponsor:** F. Hoffmann-La Roche Ltd.

**Drug Studied:** GA101 (Obinutuzumab)

**National Clinical Trial #:** NCT01287741

**EudraCT #:** 2010-024194-39

**Protocol #:** BO21005

**Results from Study Dates:** July 2011 to April 2016

**Study Title:** A Phase III, Multicenter, Open-Label Randomized Trial Comparing the Efficacy of GA101 (RO5072759) in Combination with CHOP (G-CHOP) Versus Rituximab and CHOP (R-CHOP) in Previously Untreated Patients With CD20-Positive Diffuse Large B-Cell Lymphoma (DLBCL)

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## *Thank you!*

As a clinical study participant, you belong to a large community of participants around the world. You help researchers answer important health questions and discover new medical treatments.

Thank you for taking part in the global clinical study for the drug obinutuzumab. The treatment was studied for use in patients with a type of Non-Hodgkin's Lymphoma called diffuse large B-cell lymphoma, also called DLBCL.

Your study is still ongoing. F. Hoffmann-La Roche, the sponsor of this study, thinks it is important for you to know the main results so far. The sponsors asked an independent non-profit organization called CISCRP and a medical writing organization called Synchrogenix to help prepare this summary for you. We hope it helps you understand the results and makes you feel proud of your important role in medical research. If you have questions about the results, please speak with your doctor, research nurse, or other team member at your clinic or hospital.

## What's happened since you joined the study?

The study you are involved with began in July 2011, although you may have joined this study at a later time. This summary tells you the results for all patients worldwide up to April 2016. The initially planned number of patients has been included in the study, but the study is still ongoing, and study doctors are still collecting information.

A total of 1418 patient with previously untreated DLBCL were enrolled in the study, and 1407 patients at 207 clinics or hospitals received at least 1 dose of a study drug. Eleven patients left the study before receiving any study treatment. The sponsor pre-planned to review the data collected by April 2016 and created a report of the results. This is a summary of that report.

## Why was the research needed?

Researchers were looking for a different way to treat an aggressive type of blood cancer called diffuse large B-cell lymphoma, also called DLBCL. In people with DLBCL, cancer starts in a type of cell in their blood called a B cell.

Obinutuzumab is a drug that may help destroy B cells. Obinutuzumab is a type of antibody. Antibodies are normally made by the body's immune system to fight off infection and keep you healthy, but they can also be made in a laboratory to treat a variety of diseases, including DLBCL. Obinutuzumab attaches itself to a protein called CD20 that is found on the surface of cancer and normal B cells. Rituximab is another antibody drug that targets CD20 and has already been approved to treat previously untreated DLBCL.

The standard treatment for lymphoma includes combining antibody drugs like rituximab with other drugs that treat cancer, called chemotherapy drugs. In this study, researchers wanted to compare how well obinutuzumab worked to treat your cancer compared to a drug called rituximab when these two drugs were combined with a standard chemotherapy used in previously untreated DLBCL.

This study enrolled men and women who were at least 18 years old. All of them had DLBCL that had not been treated before and had tumors that were positive for CD20.

In this study, researchers wanted to learn:

- Did fewer patients who received obinutuzumab have their cancer get worse or come back compared to patients who received rituximab?
- Did patients who received obinutuzumab live longer compared to patients who received rituximab?
- Was obinutuzumab treatment different from rituximab treatment in other ways?
- What adverse events did patients have? An adverse event is a medical problem that may or may not be caused by the study drug.

## What kind of study was this?

Your study was “open-label”. This means that the patients, doctors, and study staff knew what drugs patients were receiving. Your study was also “randomized”, which means that patients in your study were randomly assigned to receive obinutuzumab with chemotherapy or rituximab with chemotherapy. Some studies are done this way to make sure that the results are actually due to the study drug and not because of things like patients’ age or other factors.

## What happened during the study?

**Before the study began**, patients had a full check-up done to see if they could join the study. This included an electrocardiogram or ECG to check the health of their heart. Patients also had images of their tumors, samples of their bone marrow, and a sample of tumor taken.

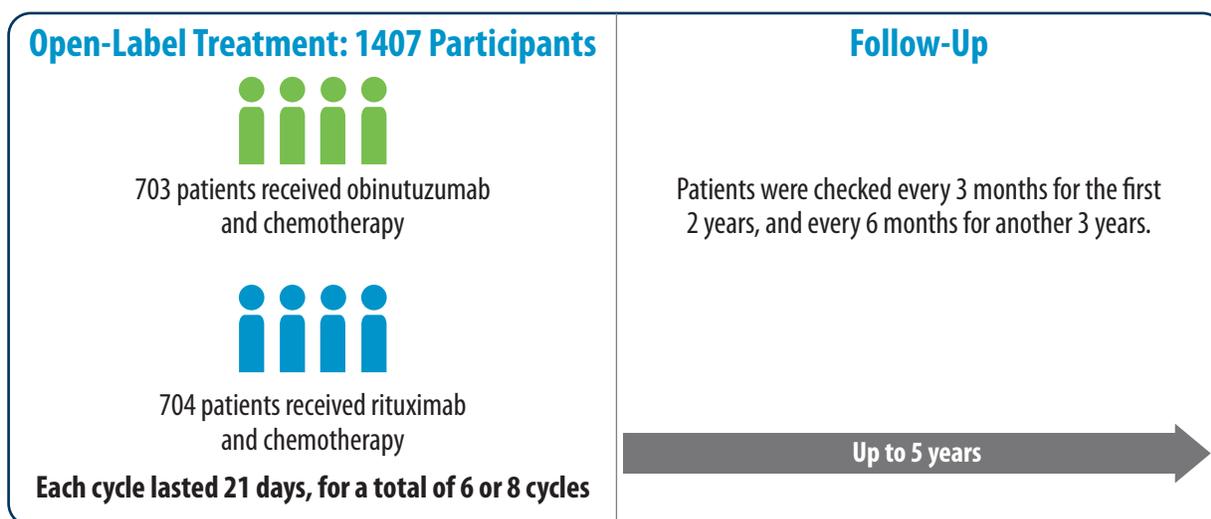
Patients also had blood and urine samples taken.

**Patients were treated for about 6 months.** Patients received a chemotherapy drug and either obinutuzumab or rituximab. The doses of the study drug and how often patients received the dose were decided based on previous studies. The dose of rituximab is considered standard and what is typically given to patients with DLBCL. Patients received the study treatments by IV, which means the treatment was injected into a vein using a needle.

There were 6 or 8 treatment cycles, depending on which clinic or hospital patients went to. Each cycle lasted 21 days. Patients who received obinutuzumab got it on Days 1, 8, and 15 of the first treatment cycle and on Day 1 of the rest of their cycles. Patients who were assigned to receive rituximab got it only on Day 1 of their treatment cycles. For those patients who had 6 treatment cycles, patients received obinutuzumab or rituximab without chemotherapy for the last 2 treatment cycles.

The figure below shows what happened during each treatment cycle.

### Treatment Cycle in This Study



At regularly scheduled points in the study, study doctors took images of patients' tumors to see how they were responding to the treatments. Patients were also asked about their quality of life at each visit to the clinic or hospital.

**After patients completed up to 8 treatment cycles**, they continued to return to the clinic every 3 months for 2 years, then every 6 months for another 3 years. During these visits, which are still ongoing, study doctors continue to check patients' tumor responses and ask patients to complete a questionnaire about their quality of life.

## What were the study results?

This section is a summary of the main results for all patients worldwide up to April 2016. It is important to know that researchers and regulatory health authorities look at the results of many studies to decide which medicines work best and are safest for patients.

### Did fewer patients who received obinutuzumab with chemotherapy have their cancer get worse or come back compared to patients who received rituximab with chemotherapy?

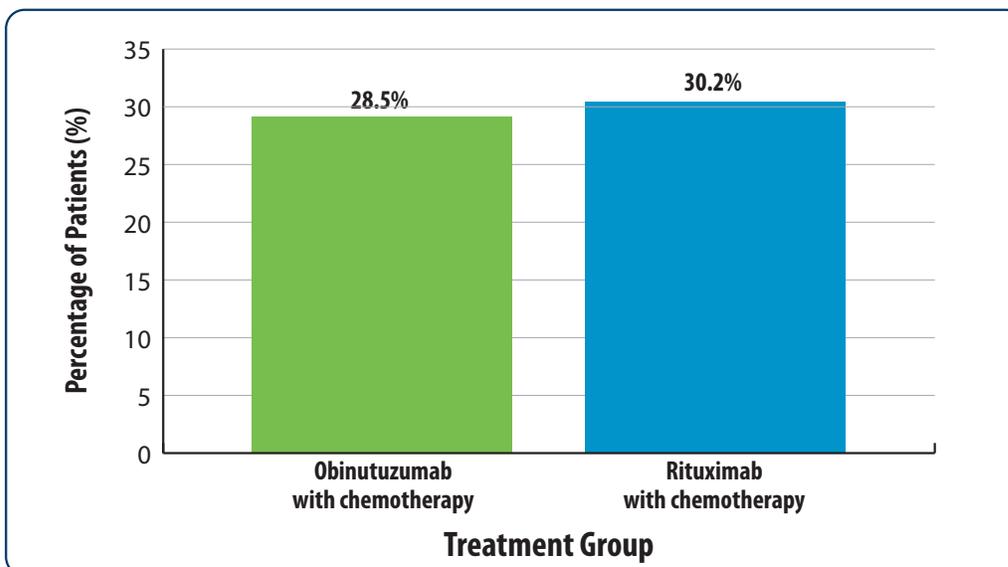
No. At the time data were analyzed, researchers found that about the same number of patients in both groups had their cancer get worse or come back. In this study, “get worse” meant that new lesions appeared, their tumors increased in size, or they died for any reason:

- 201 of 706 patients (28.5%) in the group that took obinutuzumab had their cancer get worse or come back.
- 215 of 712 patients (30.2%) in the group that took rituximab had their cancer get worse or come back.

The difference between treatment groups was not large enough for research to know if obinutuzumab was better than rituximab.

The graph below shows these results for all patients in the study.

**Proportion of Patients Whose Cancer Got Worse or Came Back**



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

No. At the time data were analyzed, researchers found that about the same number of patients in the obinutuzumab group were alive during the study compared to patients in the rituximab group:

- 580 of 706 patients (82.2%) in the obinutuzumab group were alive.
- 586 of 712 patients (82.3%) in the rituximab group were alive.

The difference between treatment groups was not large enough for researchers to know which treatment was better.

## Was obinutuzumab with chemotherapy treatment different from rituximab with chemotherapy treatment in other ways?

No. Researchers found that the results did not show that one treatment was better than the other in the following ways:

- how patients' tumors responded to the study drugs.
- how many patients had to start a different treatment for their cancer.
- how many patients' cancer returned after they started getting better.
- how the study drugs affected patients' quality of life.

## What adverse events did patients have?

When new drugs are being studied, study doctors keep track of all of the medical problems that patients develop during the study. These medical problems are called "adverse events", and may or may not be caused by the study drug. This section tells you about the adverse events that happened in your study.

### How many patients had adverse events?

Most patients had at least 1 adverse event. Some adverse events were serious, and some were not. An adverse event is called serious, for example, when it is life-threatening, makes you go to the hospital, or causes lasting problems. Some patients stopped taking the study drugs because of an adverse event.

The table below shows how many patients had adverse events in both groups out of all patients who received treatment in this study. It also shows how many stopped taking study drugs because of adverse events.

<b>Adverse Events in this Study</b>		
	<b>Obinutuzumab with chemotherapy (Out of 704 patients)</b>	<b>Rituximab with chemotherapy (Out of 703 patients)</b>
<b>Had at least 1 adverse event</b>	683 (97.0%)	657 (93.5%)
<b>Had at least 1 serious adverse event</b>	300 (42.6%)	264 (37.6%)
<b>Stopped taking study drugs because of an adverse event</b>	84 (11.9%)	60 (8.5%)

### **What were the most common serious adverse events, and did any patients die during the study?**

The most common serious adverse event was low levels of neutrophils (a type of white blood cell) with a fever. The table below shows the serious adverse events as reported by study doctors that happened to at least 5% of patients. There were other serious adverse events, but fewer patients had them.

<b>Common Serious Adverse Events in this Study</b>		
	<b>Obinutuzumab with chemotherapy (Out of 704 patients)</b>	<b>Rituximab with chemotherapy (Out of 703 patients)</b>
<b>Low levels of neutrophils (type of white blood cell) with a fever</b>	81 (11.5%)	72 (10.2%)
<b>Low levels of neutrophils (type of white blood cell)</b>	52 (7.4%)	40 (5.7%)
<b>Pneumonia (infection in the lungs)</b>	40 (5.7%)	32 (4.6%)

Overall, 41 out of 704 (5.8%) in the obinutuzumab group and 30 out of 703 patients (4.3%) in the rituximab group died during the study because of adverse events.

## What were the most common adverse events?

The most common adverse event was low levels of neutrophils (a type of white blood cell). The table below shows the most common adverse events as reported by study doctors that happened to at least 15% of patients. There were other adverse events, but fewer patients had them.

<b>Most Common Adverse Events in this Study</b>		
<b>Adverse Event</b>	<b>Obinutuzumab with chemotherapy (Out of 704 patients)</b>	<b>Rituximab with chemotherapy (Out of 703 patients)</b>
<b>Low levels of neutrophils (type of white blood cell)</b>	340 (48.3%)	286 (40.7%)
<b>Reaction at the site of the injection</b>	254 (36.1%)	165 (23.5%)
<b>Nausea</b>	207 (29.4%)	199 (28.3%)
<b>Constipation</b>	165 (23.4%)	172 (24.5%)
<b>Alopecia (sudden hair loss)</b>	145 (20.6%)	142 (20.2%)
<b>Fever</b>	142 (20.2%)	83 (11.8%)
<b>Tiredness</b>	137 (19.5%)	123 (17.5%)
<b>Chills</b>	133 (18.9%)	37 (5.3%)
<b>Low levels of neutrophils (type of white blood cell) with a fever</b>	127 (18.0%)	108 (15.4%)
<b>Low levels of white blood cells</b>	115 (16.3%)	87 (12.4%)
<b>Diarrhea</b>	112 (15.9%)	92 (13.1%)

## What is important to know about these results?

In this study, researchers compared obinutuzumab with chemotherapy to rituximab with chemotherapy in patients with previously untreated DLBCL. They found that about the same number of patients who received obinutuzumab with chemotherapy had their cancer get worse or come back compared to patients who received rituximab with chemotherapy. The difference between the 2 treatment groups was not large enough to suggest that obinutuzumab with chemotherapy was better than rituximab with chemotherapy. This study is still ongoing, and study doctors are still collecting information. Overall, researchers found that the adverse events in this study were comparable to what has been shown in previous studies with obinutuzumab.

## Where can you learn more about this study?

You can find more information about your study online at

- <https://clinicaltrials.gov/ct2/show/results/NCT01287741>
- <https://www.clinicaltrialsregister.eu/ctr-search/search?query=2010-024194-39>

Please also refer to the informed consent form you signed before joining this study for more details about your study.

If you have questions about the results, please speak with the doctor, research nurse, or other team member at your clinic or hospital.

**It takes patients in many studies all around the world to advance medical science.**

Address and contact information for the sponsor of this trial:

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## Thank you

It is said that the greatest gift is one that is given anonymously, given when you do not know whether you will get direct personal benefit.

This is the gift that you have given by taking part in a clinical trial. It is a brave and selfless act, one that advances medical knowledge. Thank you for the gift of your participation in clinical research.



The Center for Information & Study on Clinical Research Participation (CISCRP) is a non-profit organization focused on educating and informing the public about clinical research participation. CISCRP is not involved in recruiting patients for clinical trials, nor is it involved in conducting clinical trials.

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