Clinical Trial RESULTS

Research Sponsor: F. Hoffmann-La Roche Ltd.

Drug Studied: GA101 (Obinutuzumab)

National Clinical Trial #: NCT01332968

EudraCT #: 2010-024132-41

Protocol #: BO21223

Results from Study Dates: July 2011 to January 2016

Study Title: 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

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 study drug obinutuzumab. The treatment was studied for use in patients with 2 types of Non-Hodgkin's lymphoma, also called NHL.

Your study is still ongoing. F. Hoffmann-La Roche, the sponsor of this study, thinks it is important for you to know the results so far. The sponsor 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 January 2016. The initially planned number of patients has been included in the study, but the study is ongoing and study doctors are still collecting information for several years to come.

A total of 1,401 patients from 18 countries around the world are enrolled in the study, and 1,390 patients at 177 clinics or hospitals received at least one dose of a study drug. The sponsor pre-planned to review the data collected by January 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 a certain type of slow-growing cancer called Non-Hodgkin's lymphoma, also called NHL. People with this disease have higher levels of a type of white blood cell in their body, called a B cell. The most common type of NHL is follicular lymphoma, also called FL. Most of the patients in the study had previously untreated FL, but some patients had a different kind of NHL called marginal zone lymphoma or MZL.

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 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 cancer and normal B cells.

A 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 one of the three standard chemotherapies. Rituximab is another antibody drug that targets CD20 and is often considered routine care for your 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 slow-growing NHL, including FL, 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?
- Did fewer patients who received obinutuzumab have to start a new or different treatment for their cancer compared to patients who received rituximab?
- How did the study treatments affect patients' quality of life?
- 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 were randomly assigned to receive obinutuzumab with chemotherapy or rituximab with chemotherapy. Some studies are done this way to help make sure that the results are actually due to the study drug and not because of things like patients' age, disease status, or other reasons.

What happened during the study?

Before the study began, your doctor selected one of three chemotherapies that was given together with your antibody treatment:

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

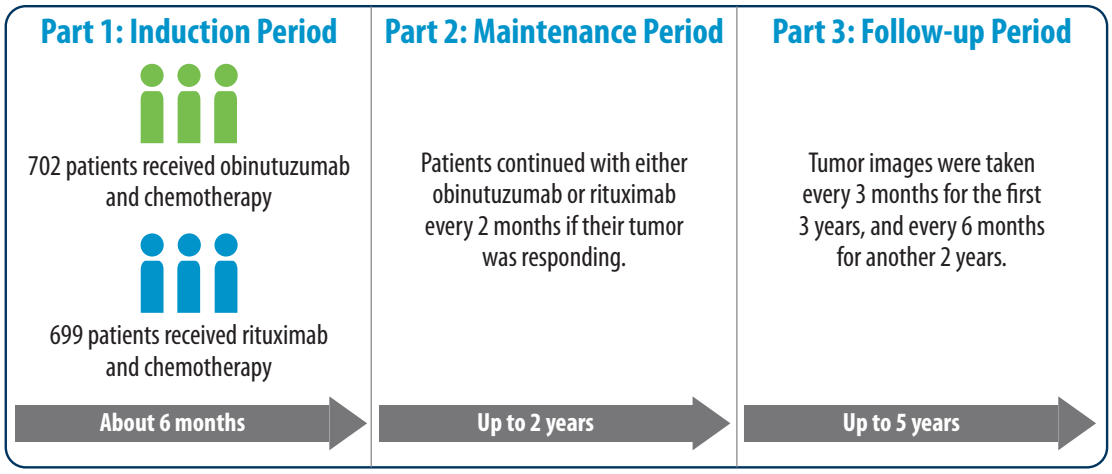
Part 1 of your treatment lasted up to 8 months and is called the "Induction Period". During Part 1, patients received chemotherapy and either obinutuzumab or rituximab. Patients received the study treatments by mouth or intravenously which means the treatment was injected into a vein using a needle.

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

Part 2 lasted up to 2 years and is called the "Maintenance Period". After patients finished Part 1 of the study, study doctors checked how patients' tumors responded to the treatment. Patients could move on to Part 2 if their tumor 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, without any chemotherapy drugs.

Part 3 is called the "Follow-up Period and is ongoing at the moment". Patients were and are still 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 take images of tumors to see how they are responding to the treatments, perform exams and ask how the patient was feeling.

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



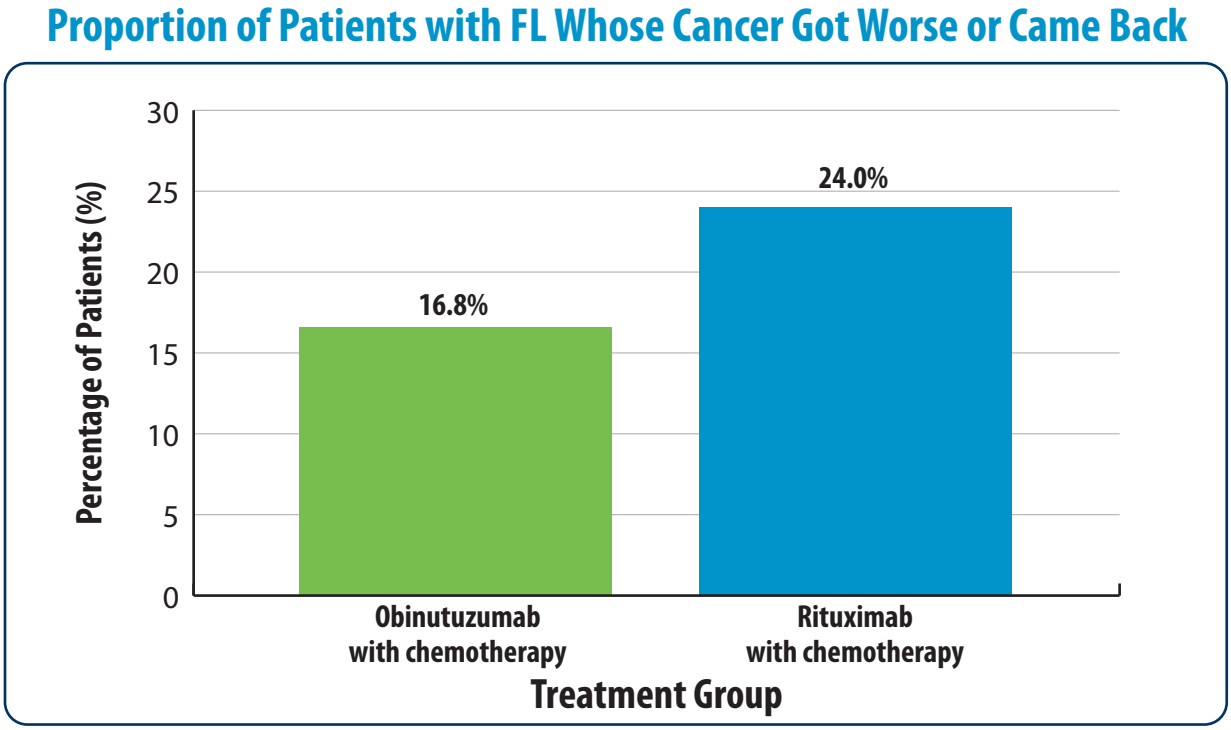
What were the study results?

This section is a summary of the results for all patients worldwide up to January 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?

Yes, researchers found that fewer patients who received obinutuzumab with chemotherapy had their cancer get worse or come back compared with patients who received rituximab with chemotherapy. In this study, "get worse" meant that new lesions appeared, their tumors increased in size, or they died for any reason. A total of 101 of 601 (16.8%) patients with FL had their cancer get worse or come back in the obinutuzumab group compared to 144 of 601 (24.0%) patients with FL in the rituximab group.

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



The results were similar when researchers looked at all patients in the study, including the patients with MZL. Fewer patients in the obinutuzumab group had their cancer get worse or come back compared to patients in the rituximab group:

- 122 of 702 (17.4%) patients in the obinutuzumab group
- 171 of 699 (24.5%) patients in the rituximab group

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

At the time data were analyzed, researchers found that more patients in the obinutuzumab group were alive compared to the number of patients in the rituximab group:

- 652 of 702 (92.9%) patients in the obinutuzumab group were alive
- 636 of 699 (91.0%) patients in the rituximab group were alive

However, the follow-up time in this study is not long enough to see if patients in one treatment group live longer than the other treatment group.

The results were similar when researchers looked only at patients in the study with FL.

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?

If patients' tumors come back or get worse, they may have to start a new or different treatment for their cancer. At the time data were analyzed, researchers found that fewer patients in the obinutuzumab group had to start a different treatment (because their tumors came back or worsened) for their lymphoma compared to patients in the rituximab group:

- 103 of 702 (14.7%) patients in the obinutuzumab group
- 138 of 699 (19.7%) patients in the rituximab group

How did the study treatments affect patients' quality of life?

Researchers used 2 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 differences between the two treatment groups in 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 worldwide.

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 considered 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 a serious adverse event.

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

Adverse Events in this Study

	All Patients (FL and MZL)		Patients with FL	
	Obinutuzumab with chemotherapy (Out of 698 patients)	Rituximab with chemotherapy (Out of 692 patients)	Obinutuzumab with chemotherapy (Out of 595 patients)	Rituximab with chemotherapy (Out of 597 patients)
Had at least 1 adverse event	695 (99.6%)	682 (98.6%)	592 (99.5%)	587 (98.3%)
Had at least 1 serious adverse event	340 (48.7%)	286 (41.3%)	274 (46.1%)	238 (39.9%)
Stopped taking any study drug because of an adverse event	125 (17.9%)	104 (15.0%)	97 (16.3%)	85 (14.2%)

What were the most common serious adverse events?

The table below shows the most common serious adverse events as reported by study doctors, which happened to at least 3% of patients. There were other serious adverse events, but fewer patients had them.

Serious Adverse Events in this Study

	All Patients (FL and MZL)		Patients with FL	
Serious Adverse Event	**Obinutuzumab with chemotherapy (Out of 698 patients)**	**Rituximab with chemotherapy (Out of 692 patients)**	**Obinutuzumab with chemotherapy (Out of 595 patients)**	**Rituximab with chemotherapy (Out of 597 patients)**
Pneumonia (infection in the lungs)	42 (6.0%)	30 (4.3%)	29 (4.9%)	25 (4.2%)
Fever	37 (5.3%)	24 (3.5%)	18 (3.0%)	17 (2.8%)
Reaction related to the IV infusion	36 (5.2%)	18 (2.6%)	27 (4.5)	11 (1.8%)
Fever associated with a low white blood cell count	34 (4.9%)	24 (3.5%)	29 (4.9%)	19 (3.2%)
Low white blood cell count	25 (3.6%)	30 (4.3%)	22 (3.7%)	25 (4.2%)

Overall, 36 out of 698 patients (5.2%) in the obinutuzumab group and 26 out of 692 patients (3.8%) in the rituximab group died during the study because of adverse events. Among the FL patients, 24 out of 595 patients (4.0%) in obinutuzumab group and 20 out of 597 patients (3.4%) in rituximab group died during this study due to adverse events.

What were the most common adverse events?

The table below shows the most common adverse events as reported by study doctors that happened to at least 25% of patients. There were other adverse events, but fewer patients had them.

Most Common Adverse Events in this Study

	All Patients (FL and MZL)		Patients with FL	
Adverse Event	Obinutuzumab with chemotherapy (Out of 698 patients)	Rituximab with chemotherapy (Out of 692 patients)	Obinutuzumab with chemotherapy (Out of 595 patients)	Rituximab with chemotherapy (Out of 597 patients)
Reaction related to the IV infusion	426 (61.0%)	339 (49.0%)	351 (59.0%)	292 (48.9%)
Low white blood cell count	336 (48.1%)	298 (43.1%)	289 (48.6%)	260 (43.6%)
Nausea	330 (47.3%)	313 (45.2%)	279 (46.9%)	278 (46.6%)
Tiredness	259 (37.1%)	247 (35.7%)	214 (36.0%)	218 (36.5%)
Constipation	240 (34.4%)	205 (29.6%)	210 (35.3%)	188 (31.5%)
Fever	209 (29.9%)	156 (22.5%)	164 (27.6%)	127 (21.3%)
Diarrhea	190 (27.2%)	154 (22.3%)	160 (26.9%)	131 (21.9%)
Cough	194 (27.8%)	165 (23.8%)	152 (25.5%)	144 (24.1%)

What is important to know about these results?

In this study, researchers compared obinutuzumab plus chemotherapy to rituximab plus chemotherapy in patients with different types of NHL. They found that fewer patients who received obinutuzumab plus chemotherapy had their cancer get worse or come back compared to patients who received rituximab plus chemotherapy. However, this study is still ongoing, and study doctors are still collecting information. It is too early in the study to know for certain if patients who received obinutuzumab plus chemotherapy live longer than patients who received rituximab plus chemotherapy. 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/NCT01332968
- https://www.clinicaltrialsregister.eu/ctr-search/search?query=2010-024132-41

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.

CISCRP
THE CENTER FOR INFORMATION & STUDY ON CLINICAL RESEARCH PARTICIPATION

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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