ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 08/15/2014

ClinicalTrials.gov ID: NCT00576758

Study Identification

Unique Protocol ID:	BO21003
Brief Title:	GAUSS: A Study of Obinutuzumab (RO5072759) in Patients With Indolent Non-Hodgkin's Lymphoma
Official Title:	An Open-label, Multi-center, Randomized Study to Evaluate the Efficacy on Tumor Response of GA101 (RO5072759) Monotherapy Versus Rituximab Monotherapy in Patients With Relapsed CD20+ Indolent Non-Hodgkin's Lymphoma
Secondary IDs:	

Study Status

Record Verification:	August 2014
Overall Status:	Completed
Study Start:	January 2008
Primary Completion:	September 2011 [Actual]
Study Completion:	March 2013 [Actual]

Sponsor/Collaborators

Sponsor:	Hoffmann-La Roche
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	No
IND/IDE Protocol?:	No

Review Board:	Approval Status: Approved Approval Number: 07-120 Board Name: Bureau d'ethique de la recherche Board Affiliation: Jewish General Hospital Phone: 541-340-82220 x2445 Email: carolyn.ells@mcgill.ca
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Canada: Health Canada

Study Description

Brief Summary:	This study will investigate the efficacy of weekly intravenous obinutuzumab [GA101 (RO5072759)] monotherapy, in patients with relapsed CD20+ indolent Non-Hodgkin's Lymphoma. Patients will be randomized to receive either GA101 or rituximab, given as four weekly infusions. At the conclusion of the initial trial patients may be eligible to continue therapy up to 24 months. The anticipated time on study treatment is 3- 24 months, and the target sample size is 100-500 individuals.
Detailed Description:	

Conditions

Conditions:	Non-Hodgkin's Lymphoma
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2
Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Open Label
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	175 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Obinutuzumab Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.	Drug: obinutuzumab (RO5072759) 1000 mg obinutuzumab intravenous (IV) infusion once a week for 4 weeks. Other Names: • RO5072759 • GA101 • GAZYVA®
Active Comparator: Rituximab Participants received 375 mg/m^2 rituximab IV infusion once a week on Days 1, 8, 15 and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression were eligible to receive a 375 mg/m^2 rituximab IV infusion once every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.	Drug: rituximab 375 mg/m^2 rituximab IV infusion once a week for 4 weeks.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- adult patients, >=18 years of age
- relapsed CD20+ indolent B-cell non-Hodgkin's lymphoma
- documented history of response of >/= 6 months duration from last rituximab-containing regimen
- clinical indication for treatment as determined by the investigator
- Eastern Cooperative Oncology Group (ECOG) performance status 0-2

Exclusion Criteria:

- prior use of any investigational monoclonal antibody within 6 months of study start

- prior use of any anti-cancer vaccine
- prior use of rituximab within 8 weeks of study entry
- radioimmunotherapy within 3 months prior to study entry
- Central Nervous System (CNS) lymphoma or evidence of transformation to high-grade or diffuse large B-cell lymphoma

Contacts/Locations

Study Officials: Clinical Trials
Study Director
Hoffmann-La Roche

Locations: United States, Washington
Seattle, Washington, United States, 98109

Spain
Valencia, Valencia, Spain, 46010

United States, North Carolina
Concord, North Carolina, United States, 28025

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Croatia
Rijeka, Croatia, 51000

Argentina
Buenos Aires, Argentina, 1406

Brazil
Goiania, GO, Brazil, 74140-050

Turkey
Istanbul, Turkey, 34365

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Rituximab	Participants received 375 mg/m^2 rituximab IV infusion once a week on Days 1, 8, 15 and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression were eligible to receive a 375 mg/m^2 rituximab IV infusion once every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Induction Treatment Period

	Rituximab	Obinutuzumab
Started	87	88
Received Treatment	86	87
Completed	79	83
Not Completed	8	5
Adverse event or Intercurrent illness	3	3
Insufficient therapeutic response	2	0
Violation of selection criteria at entry	1	1
Death	1	0

	Rituximab	Obinutuzumab
Refused treatment/ Did not Cooperate	0	1
Withdrew consent	1	0

Extension Treatment Period

	Rituximab	Obinutuzumab
Started	72 [1]	73 [2]
Completed	30 [3]	30
Not Completed	42	43
Adverse event or Intercurrent illness	6	7
Death	1	1
Refused treatment/did not cooperate	2	1
Insufficient therapeutic response	30	33
Administrative/Other	3	1

[1] 6 patients did not enter extended treatment phase/follow-up + 1 patient entered follow-up.
[2] 8 patients did not enter extended treatment phase/follow-up phase + 2 patients entered follow-up.
[3] + 2 patients (pts) who withdrew prior to receiving study drug.

Follow-up Period

	Rituximab	Obinutuzumab
Started	55 [1]	51 [2]
Completed	28	34
Not Completed	27	17
Administrative/Other	6	8
Death	3	3
Insufficient therapeutic response	16	5
Withdrew consent	2	1

[1] Includes 23 pts who entered follow-up after induction and didn't enter the extended treatment phase.
[2] Includes 21 pts who entered follow-up after induction and didn't enter the extended treatment phase.

Baseline Characteristics

Reporting Groups

	Description
Rituximab	Participants received 375 mg/m^2 rituximab IV infusion once a week on Days 1, 8, 15 and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression were eligible to receive a 375 mg/m^2 rituximab IV infusion once every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Baseline Measures

	Rituximab	Obinutuzumab	Total
Number of Participants	87	88	175
Age, Customized [units: participants]			
<65 years	49	47	96
65-70 years	22	22	44
>70 years	16	19	35
Gender, Male/Female [units: participants]			
Female	43	42	85
Male	44	46	90

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants With Overall Response At the End of Induction Period

Measure Description	Overall response was defined as Complete Response (CR), Complete Response/Unconfirmed (CRu) or Partial Response (PR) as assessed by investigator at end of induction treatment. Computed tomography imaging was used for the primary assessment of tumor response per 1999 criteria by Cheson. CR was defined as the disappearance of all clinical and radiographic evidence of disease, disease-related symptoms and normalization of biochemical abnormalities of NHL. CRu was CR plus one or more of the following: A residual lymph node mass greater than 1.5 cm in greatest transverse diameter that has regressed by more than 75% in the sum of the products of the greatest diameter (tumors)(SPD) and/ or indeterminate bone marrow. PR was defined as 50% decrease in SPD of the 6 largest dominant nodes or nodal masses. No increase in the size of the other nodes, liver, or spleen. Splenic and hepatic nodules must regress by at least 50% in the SPD. No new sites of disease.
Time Frame	Randomization to clinical cutoff: 01 September 2011 (Up to 70 days)
Safety Issue?	No

Analysis Population Description

Participants from the Intent-to-treat (ITT) population (all randomized participants) with follicular non-Hodgkin's lymphoma (NHL) at the time of diagnosis.

Reporting Groups

	Description
Rituximab	Participants received 375 mg/m^2 rituximab IV infusion once a week on Days 1, 8, 15 and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression were eligible to receive a 375 mg/m^2 rituximab IV infusion once every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Measured Values

	Rituximab	Obinutuzumab
Number of Participants Analyzed	75	74
Percentage of Participants With Overall Response At the End of Induction Period [units: Percentage of participants]	33.3	44.6

Statistical Analysis 1 for Percentage of Participants With Overall Response At the End of Induction Period

Statistical Analysis Overview	Comparison Groups	Rituximab, Obinutuzumab
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1587
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	11.26
	Confidence Interval	(2-Sided) 60% 3.9 to 18.7
	Estimation Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Complete Response at the End of the Induction Period
Measure Description	Computed tomography imaging was used for the primary assessment of tumor response per 1999 criteria by Cheson. CR is defined as the disappearance of all clinical and radiographic evidence of disease, disease-related symptoms and normalization of biochemical abnormalities of NHL. All lymph nodes and nodal masses must have regressed to normal size. The spleen, if considered to be enlarged before therapy on the basis of a CT scan, must have regressed in size and must not be palpable on physical examination. Any macroscopic nodules in any organs detectable on imaging techniques should no longer be present. Other organs considered to be enlarged before therapy due to involvement by lymphoma, such as liver and kidneys, must have decreased in size. If the bone marrow was involved by lymphoma before treatment, the infiltrate must be cleared on repeat bone marrow aspirate and biopsy of the same site.
Time Frame	Randomization to clinical cutoff : 01 September 2011 (Up to 70 days)
Safety Issue?	No

Analysis Population Description

Participants from the Intent-to-treat (ITT) population (all randomized participants) with follicular non-Hodgkin's lymphoma (NHL) at the time of diagnosis.

Reporting Groups

	Description
Rituximab	Participants received 375 mg/m^2 rituximab IV infusion once a week on Days 1, 8, 15 and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression were eligible to receive a 375 mg/m^2 rituximab IV infusion once every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Measured Values

	Rituximab	Obinutuzumab
Number of Participants Analyzed	75	74
Percentage of Participants With Complete Response at the End of the Induction Period [units: Percentage of participants] Number (95% Confidence Interval)	5.3 (1.5 to 13.1)	12.2 (5.7 to 21.8)

Statistical Analysis 1 for Percentage of Participants With Complete Response at the End of the Induction Period

Statistical Analysis Overview	Comparison Groups	Rituximab, Obinutuzumab
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	6.83
	Confidence Interval	(2-Sided) 95% -2.9 to 16.6
	Estimation Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Partial Response (PR) at the End of the Induction Period
Measure Description	Computed tomography imaging was used for the primary assessment of tumor response per 1999 criteria by Cheson. PR was defined as 50% decrease in SPD of the 6 largest dominant nodes or nodal masses. No increase in the size of the other nodes, liver, or spleen. Splenic and hepatic nodules must regress by at least 50% in the SPD. No new sites of disease.
Time Frame	Randomization to clinical cutoff : 01 September 2011 (Up to 70 days)
Safety Issue?	No

Analysis Population Description

Participants from the Intent-to-treat (ITT) population (all randomized participants) with follicular non-Hodgkin's lymphoma (NHL) at the time of diagnosis.

Reporting Groups

	Description
Rituximab	Participants received 375 mg/m^2 rituximab IV infusion once a week on Days 1, 8, 15 and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression were eligible to receive a 375 mg/m^2 rituximab IV infusion once every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Measured Values

	Rituximab	Obinutuzumab
Number of Participants Analyzed	75	74
Percentage of Participants With Partial Response (PR) at the End of the Induction Period [units: Percentage of participants] Number (95% Confidence Interval)	28.0 (18.2 to 39.6)	32.4 (22.0 to 44.3)

4. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Best Overall Response Achieved at Any Time During the Study Treatment

Measure Description	Overall response was defined as Complete Response (CR), Complete Response/Unconfirmed (CRu) or Partial Response (PR) as assessed by investigators during study treatment (induction or extended treatment phase). Computed tomography imaging was used for the primary assessment of tumor response per 1999 criteria by Cheson. CR was defined as the disappearance of all clinical and radiographic evidence of disease, disease-related symptoms and normalization of biochemical abnormalities of NHL. CRu was CR plus one or more of the following: A residual lymph node mass greater than 1.5 cm in greatest transverse diameter that has regressed by more than 75% in the sum of the products of the greatest diameter (tumors)(SPD) and/ or indeterminate bone marrow. PR was defined as 50% decrease in SPD of the 6 largest dominant nodes or nodal masses. No increase in the size of the other nodes, liver, or spleen. Splenic and hepatic nodules must regress by at least 50% in the SPD. No new sites of disease.
Time Frame	Randomization to clinical cutoff : 01 September 2011 (Up to 70 days)
Safety Issue?	No

Analysis Population Description

Participants from the Intent-to-treat (ITT) population (all randomized participants) with follicular non-Hodgkin's lymphoma (NHL) at the time of diagnosis.

Reporting Groups

	Description
Rituximab	Participants received 375 mg/m^2 rituximab IV infusion once a week on Days 1, 8, 15 and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression were eligible to receive a 375 mg/m^2 rituximab IV infusion once every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Measured Values

	Rituximab	Obinutuzumab
Number of Participants Analyzed	75	74
Percentage of Participants With Best Overall Response Achieved at Any Time During the Study Treatment [units: Percentage of participants] Number (95% Confidence Interval)		

	Rituximab	Obinutuzumab
Complete Response	18.7 (10.6 to 29.3)	35.1 (24.4 to 47.1)
Partial Response	45.3 (33.8 to 57.3)	31.1 (20.8 to 42.9)
Stable Disease	26.7 (17.1 to 38.1)	21.6 (12.9 to 32.7)
Progressive Disease	5.3 (1.5 to 13.1)	8.1 (3.0 to 16.8)

5. Secondary Outcome Measure:

Measure Title	Number of Participants With Improved Overall Response During the Extended Treatment Period
Measure Description	Overall response was defined as Complete Response (CR), Complete Response/Unconfirmed (CRu) or Partial Response (PR) as assessed by investigators at end of induction treatment. Computed tomography imaging was used for the primary assessment of tumor response per 1999 criteria by Cheson.
Time Frame	Randomization to Clinical cutoff: 07 March 2013 (Up to 43.2 months)
Safety Issue?	No

Analysis Population Description

Participants from the Intent-to-treat (ITT) population (all randomized participants) with follicular non-Hodgkin's lymphoma (NHL) at the time of diagnosis who received treatment in the extension period.

Reporting Groups

	Description
Rituximab	Participants received 375 mg/m^2 rituximab IV infusion once a week on Days 1, 8, 15 and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression were eligible to receive a 375 mg/m^2 rituximab IV infusion once every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Measured Values

	Rituximab	Obinutuzumab
Number of Participants Analyzed	63	62

	Rituximab	Obinutuzumab
Number of Participants With Improved Overall Response During the Extended Treatment Period [units: Participants]	31	32

6. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Best Overall Response Achieved at Any Time During the Study Treatment
Measure Description	Overall response was defined as Complete Response (CR), Complete Response/Unconfirmed (CRu) or Partial Response (PR) as assessed by investigators during study treatment (induction or extended treatment phase). Computed tomography imaging was used for the primary assessment of tumor response per 1999 criteria by Cheson. CR was defined as the disappearance of all clinical and radiographic evidence of disease, disease-related symptoms and normalization of biochemical abnormalities of NHL. CRu was CR plus one or more of the following: A residual lymph node mass greater than 1.5 cm in greatest transverse diameter that has regressed by more than 75% in the sum of the products of the greatest diameter (tumors)(SPD) and/ or indeterminate bone marrow. PR was defined as 50% decrease in SPD of the 6 largest dominant nodes or nodal masses. No increase in the size of the other nodes, liver, or spleen. Splenic and hepatic nodules must regress by at least 50% in the SPD. No new sites of disease.
Time Frame	Randomization to Clinical cutoff: 07 March 2013 (Up to 43.2 months)
Safety Issue?	No

Analysis Population Description

Participants from the Intent-to-treat (ITT) population (all randomized participants) with follicular non-Hodgkin's lymphoma (NHL) at the time of diagnosis.

Reporting Groups

	Description
Rituximab	Participants received 375 mg/m^2 rituximab IV infusion once a week on Days 1, 8, 15 and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression were eligible to receive a 375 mg/m^2 rituximab IV infusion once every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

	Description
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Measured Values

	Rituximab	Obinutuzumab
Number of Participants Analyzed	75	74
Percentage of Participants With Best Overall Response Achieved at Any Time During the Study Treatment [units: Percentage of participants] Number (95% Confidence Interval)		
Complete Response	22.7 (13.8 to 33.8)	41.9 (30.5 to 53.9)
Partial Response	41.3 (30.1 to 53.3)	24.3 (15.1 to 35.7)
Stable Disease	26.7 (17.1 to 38.1)	21.6 (12.9 to 32.7)
Progressive Disease	5.3 (1.5 to 13.1)	8.1 (3.0 to 16.8)
No Response Assessment	4.0 (NA to NA) [1]	4.1 (NA to NA) [1]

[1] Not estimable.

Statistical Analysis 1 for Percentage of Participants With Best Overall Response Achieved at Any Time During the Study Treatment

Statistical Analysis Overview	Comparison Groups	Rituximab, Obinutuzumab
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	2.22
	Confidence Interval	(2-Sided) 95% -13.9 to 18.3

	Estimation Comments	[Not specified]

7. Secondary Outcome Measure:

Measure Title	Progression-Free Survival (PFS)
Measure Description	PFS was defined as the time from randomization to the first occurrence of progression, relapse, or death from any cause as assessed by the Investigator. Progression was defined as a ≥ 50% increase from nadir in the SPD of any previously identified abnormal node and/or the appearance of any new lesion during or at the end of therapy. Relapse was defined as the appearance of any new lesion or increase by ≥ 50% in the size of previously involved sites and/or a ≥ 50% increase in greatest diameter of any previously identified node greater than 1 cm in its short axis or in the SPD of more than one node.
Time Frame	Randomization to Clinical cutoff: 07 March 2013 (Up to 43.2 months)
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants with follicular non-Hodgkin's lymphoma at the time of diagnosis. If no PFS even occurred, PFS was censored at the date of the last tumor assessment. If no tumor assessment was available patient was censored at the date of the first study drug administration.

Reporting Groups

	Description
Rituximab	Participants received 375 mg/m^2 rituximab IV infusion once a week on Days 1, 8, 15 and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression were eligible to receive a 375 mg/m^2 rituximab IV infusion once every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Measured Values

	Rituximab	Obinutuzumab
Number of Participants Analyzed	75	74
Progression-Free Survival (PFS) [units: Days]	772 (425 to 867)	536 (394 to NA) [1]

	Rituximab	Obinutuzumab
Median (95% Confidence Interval)		

[1] Upper limit was not estimable due to insufficient number of participants with events therefore the upper confidence limit of the survival curve is above 50%.

Statistical Analysis 1 for Progression-Free Survival (PFS)

Statistical Analysis Overview	Comparison Groups	Rituximab, Obinutuzumab
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.93
	Confidence Interval	(2-Sided) 95% 0.62 to 1.44
	Estimation Comments	[Not specified]

8. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Progression-Free Survival (PFS) Events
Measure Description	The percentage of participants with progression, relapse, or death events from any cause as assessed by the Investigator. Progression was defined as a ≥ 50% increase from nadir in the SPD of any previously identified abnormal node and/or the appearance of any new lesion during or at the end of therapy. Relapse was defined as the appearance of any new lesion or increase by ≥ 50% in the size of previously involved sites and/or a ≥ 50% increase in greatest diameter of any previously identified node greater than 1 cm in its short axis or in the SPD of more than one node.
Time Frame	Randomization to Clinical cutoff: 07 March 2013 (Up to 43.2 months)
Safety Issue?	No

Analysis Population Description

Participants from the ITT population (all randomized participants) with follicular non-Hodgkin's lymphoma at the time of diagnosis. If event did not occur, PFS was censored at the date of the last tumor assessment. If no tumor assessment is available patient was censored at the date of the first study drug administration.

Reporting Groups

	Description
Rituximab	Participants received 375 mg/m^2 rituximab IV infusion once a week on Days 1, 8, 15 and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression were eligible to receive a 375 mg/m^2 rituximab IV infusion once every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Measured Values

	Rituximab	Obinutuzumab
Number of Participants Analyzed	75	74
Percentage of Participants With Progression-Free Survival (PFS) Events [units: Percentage of participants]	57.7	51.4

9. Secondary Outcome Measure:

Measure Title	Event Free Survival
Measure Description	Event-free survival (EFS) was defined as the time between date of randomization and the date of disease progression/ relapse, death, or start of a new anti-leukemic therapy. Progression was defined as a ≥ 50% increase from nadir in the SPD of any previously identified abnormal node and/or the appearance of any new lesion during or at the end of therapy. Relapse was defined as the appearance of any new lesion or increase by ≥ 50% in the size of previously involved sites and/or a ≥ 50% increase in greatest diameter of any previously identified node greater than 1 cm in its short axis or in the SPD of more than one node.
Time Frame	Randomization to Clinical cutoff: 07 March 2013 (Up to 43.2 months)
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants with follicular non-Hodgkin's lymphoma at the time of diagnosis. If no EFS event occurred, EFS was censored at the date of the last tumor assessment. If no tumor assessment is available patient was censored at the date of the first study drug administration.

Reporting Groups

	Description
Rituximab	Participants received 375 mg/m^2 rituximab IV infusion once a week on Days 1, 8, 15 and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression were eligible to receive a 375 mg/m^2 rituximab IV infusion once every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Measured Values

	Rituximab	Obinutuzumab
Number of Participants Analyzed	75	74
Event Free Survival [units: Days] Median (95% Confidence Interval)	472.0 (362 to 772)	472.0 (318 to 605)

Statistical Analysis 1 for Event Free Survival

Statistical Analysis Overview	Comparison Groups	Rituximab, Obinutuzumab
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	1.00
	Confidence Interval	(2-Sided) 95% 0.67 to 1.50
	Estimation Comments	[Not specified]

10. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Event Free Survival (EFS) Events
Measure Description	Percentage of participants with Event Free Events: disease progression/relapse, death, or start of a new anti-leukemic therapy. Progression was defined as a ≥ 50% increase from nadir in the SPD of any previously identified abnormal node and/or the appearance of any new lesion during or at the end of therapy. Relapse was defined as the appearance of any new lesion or increase by ≥ 50% in the size of previously involved sites and/or a ≥ 50% increase in greatest diameter of any previously identified node greater than 1 cm in its short axis or in the SPD of more than one node.
Time Frame	Randomization to Clinical cutoff: 07 March 2013 (Up to 43.2 months)
Safety Issue?	No

Analysis Population Description

Participants from the Intent-to-treat (ITT) population (all randomized participants) with follicular non-Hodgkin's lymphoma (NHL) at the time of diagnosis.

Reporting Groups

	Description
Rituximab	Participants received 375 mg/m^2 rituximab IV infusion once a week on Days 1, 8, 15 and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression were eligible to receive a 375 mg/m^2 rituximab IV infusion once every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Measured Values

	Rituximab	Obinutuzumab
Number of Participants Analyzed	75	74
Percentage of Participants With Event Free Survival (EFS) Events [units: Percentage of participants]	64.0	63.5

11. Secondary Outcome Measure:

Measure Title	Duration of Response
Measure Description	Duration of Response was defined as the date the response, either Complete Response (CR) or Partial Response (PR), was first recorded until the date of Disease Progression or death due to any cause. Computed tomography imaging was used for the primary assessment of tumor response per 1999 criteria by Cheson. CR was defined as the disappearance of all clinical and radiographic evidence of disease, disease-related symptoms and normalization of biochemical abnormalities of NHL. PR was defined as 50% decrease in SPD of the 6 largest dominant nodes or nodal masses. No increase in the size of the other nodes, liver, or spleen. Splenic and hepatic nodules must regress by at least 50% in the SPD. No new sites of disease. Disease Progression was defined as a ≥ 50% increase from nadir in the SPD of any previously identified abnormal node and/or the appearance of any new lesion during or at the end of therapy.
Time Frame	Randomization to Clinical cutoff: 07 March 2013 (Up to 43.2 months)
Safety Issue?	No

Analysis Population Description

Participants from the ITT population (all randomized participants with follicular NHL at the time of diagnosis N=75/74] with response. Patients with no documented progression after CR or PR will be censored at the last tumor assessment. If no assessment available patients will be censored at the first study drug.

Reporting Groups

	Description
Rituximab	Participants received 375 mg/m^2 rituximab IV infusion once a week on Days 1, 8, 15 and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression were eligible to receive a 375 mg/m^2 rituximab IV infusion once every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Measured Values

	Rituximab	Obinutuzumab
Number of Participants Analyzed	48	49
Duration of Response [units: Months]	809 (412 to NA) [1]	NA (672 to NA) [2]

	Rituximab	Obinutuzumab
Median (95% Confidence Interval)		

[1] Upper limit was not estimable due to insufficient number of participants with events therefore the upper confidence limit of the survival curve is above 50%.

[2] Median and Upper limit was not estimable due to insufficient number of participants with events therefore the upper confidence limit of the survival curve is above 50%.

12. Secondary Outcome Measure:

Measure Title	Obinutuzumab Serum PK Parameter: Terminal Half-Life (t1/2)
Measure Description	Blood was collected for Pharmacokinetic (PK) Parameters before and after dose administration of obinutuzumab in Induction Phase Cycle 4. Serum samples were sent to a central lab and were analyzed for obinutuzumab using a validated enzyme-linked immunosorbent assay (ELISA). Terminal Half-Life was calculated in days.
Time Frame	Day 22 (pre-infusion, at end of infusion, 3-6, 20-28, 66-80 hours, 6-8, 12-16, 18-24, 28-56 days post-infusion)
Safety Issue?	No

Analysis Population Description

PK Analysis Population included all participants who received obinutuzumab and had PK samples collected as per protocol. Patients with limited PK sampling time-points were excluded from the analysis.

Reporting Groups

	Description
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Measured Values

	Obinutuzumab
Number of Participants Analyzed	72
Obinutuzumab Serum PK Parameter: Terminal Half-Life (t1/2) [units: days] Mean (Standard Deviation)	41.0 (28.6)

13. Secondary Outcome Measure:

Measure Title	Obinutuzumab Serum PK Parameter: Maximum Serum Concentration (Cmax)
Measure Description	Blood was collected for PK Parameters before and after dose administration of obinutuzumab in Induction Phase Cycles 1, 2, 3 and 4. Serum samples were sent to a central lab and were analyzed for obinutuzumab using a validated enzyme-linked immunosorbent assay (ELISA). Cmax was calculated in micrograms/milliliter (µg/mL).
Time Frame	Day 1 (pre-infusion, at end of infusion, 3-6, 20-28, 66-80 hours post-infusion), Days 8 and 15 (pre-infusion, at end of infusion), Day 22 (pre-infusion, at end of infusion, 3-6, 20-28, 66-80 hours, 6-8, 12-16, 18-24, 28-56 days post-infusion)
Safety Issue?	No

Analysis Population Description

PK Analysis Population included all participants who received obinutuzumab and had PK samples collected as per protocol. Patients with limited PK sampling time-points were excluded from the analysis.

Reporting Groups

	Description
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Measured Values

	Obinutuzumab
Number of Participants Analyzed	78
Obinutuzumab Serum PK Parameter: Maximum Serum Concentration (Cmax) [units: µg/mL] Mean (Standard Deviation)	
Cycle 1 (n=74)	292 (87.4)
Cycle 2 (n=78)	448 (129)
Cycle 3 (n=77)	561 (158)
Cycle 4 (n=77)	692 (213)

14. Secondary Outcome Measure:

Measure Title	Obinutuzumab Serum PK Parameter: Area Under the Concentration Curve (AUClast)
Measure Description	Blood was collected for PK Parameters before and after dose administration of obinutuzumab in Induction Phase Cycle 4. Serum samples were sent to a central lab and were analyzed for obinutuzumab using a validated enzyme-linked immunosorbent assay (ELISA). AUClast was calculated in days* micrograms/milliliter (µg/mL)
Time Frame	Day 22 (pre-infusion, at end of infusion, 3-6, 20-28, 66-80 hours, 6-8, 12-16, 18-24, 28-56 days post-infusion)
Safety Issue?	No

Analysis Population Description

PK Analysis Population included all participants who received obinutuzumab and had PK samples collected as per protocol. Patients with limited PK sampling time-points were excluded from the analysis.

Reporting Groups

	Description
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Measured Values

	Obinutuzumab
Number of Participants Analyzed	77
Obinutuzumab Serum PK Parameter: Area Under the Concentration Curve (AUClast) [units: day*µg/mL] Mean (Standard Deviation)	23400 (10300)

15. Secondary Outcome Measure:

Measure Title	Obinutuzumab Serum PK Parameter: Clearance at Steady-State (CLss)
Measure Description	Blood was collected for PK Parameters before and after dose administration of obinutuzumab in Induction Phase Cycle 4. Serum samples were sent to a central lab and were analyzed for obinutuzumab using a validated enzyme-linked immunosorbent assay (ELISA). CLsst was calculated in milliliter/day (mL/day)
Time Frame	Day 22 (pre-infusion, at end of infusion, 3-6, 20-28, 66-80 hours, 6-8, 12-16, 18-24, 28-56 days post-infusion)
Safety Issue?	No

Analysis Population Description

PK Analysis Population included all participants who received obinutuzumab and had PK samples collected as per protocol. Patients with limited PK sampling time-points were excluded from the analysis.

Reporting Groups

	Description
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Measured Values

	Obinutuzumab
Number of Participants Analyzed	72
Obinutuzumab Serum PK Parameter: Clearance at Steady-State (CLss) [units: mL/day] Mean (Standard Deviation)	308 (470)

16. Secondary Outcome Measure:

Measure Title	Obinutuzumab Serum PK Parameter: Volume of Distribution at Steady-State (Vss)
Measure Description	Blood was collected for PK Parameters before and after dose administration of obinutuzumab in Induction Phase Cycle 4. Serum samples were sent to a central lab and were analyzed for obinutuzumab using a validated enzyme-linked immunosorbent assay (ELISA). Vss was calculated in liters (L).
Time Frame	Day 22 (pre-infusion, at end of infusion, 3-6, 20-28, 66-80 hours, 6-8, 12-16, 18-24, 28-56 days post-infusion)
Safety Issue?	No

Analysis Population Description

PK Analysis Population included all participants who received obinutuzumab and had PK samples collected as per protocol. Patients with limited PK sampling time-points were excluded from the analysis.

Reporting Groups

	Description
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Measured Values

	Obinutuzumab
Number of Participants Analyzed	72
Obinutuzumab Serum PK Parameter: Volume of Distribution at Steady-State (Vss) [units: Liter] Mean (Standard Deviation)	14.6 (9.8)

17. Secondary Outcome Measure:

Measure Title	Obinutuzumab Serum PK Parameter: Area Under the Concentration Curve Between Dosing Interval (AUCtau)
Measure Description	Blood was collected for PK Parameters before and after dose administration of obinutuzumab in Induction Phase Cycle 4. Serum samples were sent to a central lab and were analyzed for obinutuzumab using a validated enzyme-linked immunosorbent assay (ELISA). AUCtau was calculated in days* micrograms/milliliter (µg/mL)
Time Frame	Day 22 (pre-infusion, at end of infusion, 3-6, 20-28, 66-80 hours, 6-8, 12-16, 18-24, 28-56 days post-infusion)
Safety Issue?	No

Analysis Population Description

PK Analysis Population included all participants who received obinutuzumab and had PK samples collected as per protocol. Patients with limited PK sampling time-points were excluded from the analysis.

Reporting Groups

	Description
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Measured Values

	Obinutuzumab
Number of Participants Analyzed	77
Obinutuzumab Serum PK Parameter: Area Under the Concentration Curve Between Dosing Interval (AUCtau) [units: day*µg/mL] Mean (Standard Deviation)	4370 (1340)

18. Secondary Outcome Measure:

Measure Title	Obinutuzumab Trough Serum Concentration (Ctrough)
Measure Description	Blood was collected for PK Parameters before and after dose administration of obinutuzumab in Induction Phase Cycles 2, 3 and 4. Serum samples were sent to a central lab and were analyzed for obinutuzumab using a validated enzyme-linked immunosorbent assay (ELISA). Ctrough was calculated in micrograms/milliliter (µg/mL).
Time Frame	Days 8 and 15 (pre-infusion, at end of infusion), Day 22 (pre-infusion, at end of infusion, 3-6, 20-28, 66-80 hours, 6-8, 12-16, 18-24, 28-56 days post-infusion)
Safety Issue?	No

Analysis Population Description

PK Analysis Population included all participants who received obinutuzumab and had PK samples collected as per protocol. Patients with limited PK sampling time-points were excluded from the analysis.

Reporting Groups

	Description
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Measured Values

	Obinutuzumab
Number of Participants Analyzed	78
Obinutuzumab Trough Serum Concentration (Ctrough) [units: µg/mL]	

	Obinutuzumab
Mean (Standard Deviation)	
Cycle 2 (n=78)	154 (62.7)
Cycle 3 (n=77)	301 (119)
Cycle 4 (n=75)	418 (147)

19. Secondary Outcome Measure:

Measure Title	Number of Participants With Peripheral Blood B-Cell Depletion
Measure Description	Blood was collected and sent to a central laboratory for the evaluation of cluster of differentiation 19 (CD19) by flow cytometry at the end of the induction period. B-cell depletion was defined as a CD19 result 5 % of the Baseline value after at least one dose of study drug was administered.
Time Frame	Day 22
Safety Issue?	No

Analysis Population Description

Participants from the Safety Population, all randomized participants who received study drug, with data available for analysis.

Reporting Groups

	Description
Rituximab	Participants received 375 mg/m^2 rituximab IV infusion once a week on Days 1, 8, 15 and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression were eligible to receive a 375 mg/m^2 rituximab IV infusion once every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Measured Values

	Rituximab	Obinutuzumab
Number of Participants Analyzed	84	85

	Rituximab	Obinutuzumab
Number of Participants With Peripheral Blood B-Cell Depletion [units: Participants]	80	82

20. Secondary Outcome Measure:

Measure Title	Number of Participants With Peripheral Blood B-Cell Recovery
Measure Description	Blood was sent to a central laboratory for the evaluation of cluster of differentiation 19 (CD19) by flow cytometry. B-cell recovery was defined as the time point when the CD-19 values return to ≥ 50% of baseline levels. The number of participants with B-cell recovery from End of Induction (treatment) Phase to 6 months of Follow-up is reported in two categories: Recovery with Progressive Disease (PD) or Recovery without PD. PD required one of the following: 50 % increase in the absolute number of circulating lymphocytes, Appearance of new palpable lymph nodes, 50 % increase in the longest diameter of any previous site of lymphadenopathy, 50 % increase in the enlargement of the liver and/or spleen or Transformation to a more aggressive histology.
Time Frame	End of last dose + 6 Months Follow-Up
Safety Issue?	No

Analysis Population Description

Participants from the Safety Population, all randomized participants who received study drug, with previous B-Cell Depletion and B-Cell assessment at 6 Month Follow-up.

Reporting Groups

	Description
Rituximab	Participants received 375 mg/m^2 rituximab IV infusion once a week on Days 1, 8, 15 and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression were eligible to receive a 375 mg/m^2 rituximab IV infusion once every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Measured Values

	Rituximab	Obinutuzumab
Number of Participants Analyzed	69	73
Number of Participants With Peripheral Blood B-Cell Recovery [units: Participants]		
Recovery with PD	0	2
Recovery without PD	1	0

21. Secondary Outcome Measure:

Measure Title	Number of Participants With Adverse Events (AE) and Serious Adverse Events (SAE)
Measure Description	An AE was defined as any unfavorable and unintended sign (including an abnormal laboratory result), symptom, or disease temporally associated with the use of an investigational medicinal product (IMP) or other protocol-imposed intervention, regardless of attribution. A SAE was any AE that was one of the following: fatal, life-threatening, required or prolonged inpatient hospitalization, resulted in persistent or significant disability/incapacity, a congenital anomaly/ birth defect in a neonate/infant born to a mother exposed to the investigational product or considered a significant medical event by the investigator. Additional information about AEs can be found in the Adverse Event Section.
Time Frame	Randomization to Clinical cutoff: 07 March 2013 (Up to 43.2 months) [Includes all AEs reported 28 days after last dose and all Related SAEs regardless of time of last dose.]
Safety Issue?	No

Analysis Population Description

Safety Population included all randomized participants who received study drug.

Reporting Groups

	Description
Rituximab	Participants received 375 mg/m^2 rituximab IV infusion once a week on Days 1, 8, 15 and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression were eligible to receive a 375 mg/m^2 rituximab IV infusion once every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Measured Values

	Rituximab	Obinutuzumab
Number of Participants Analyzed	86	87
Number of Participants With Adverse Events (AE) and Serious Adverse Events (SAE) [units: Participants]		
AE	74	83
SAE	17	21

22. Secondary Outcome Measure:

Measure Title	Number of Participants With Infusion Related Reactions
Measure Description	Infusion Related Reactions were AEs that occurred during the infusion or within 24 hours of the infusion.
Time Frame	Randomization to Clinical cutoff: 07 March 2013 (Up to 43.2 months)
Safety Issue?	No

Analysis Population Description

Safety Population included all randomized participants who received at least once dose of study drug.

Reporting Groups

	Description
Rituximab	Participants received 375 mg/m^2 rituximab IV infusion once a week on Days 1, 8, 15 and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression were eligible to receive a 375 mg/m^2 rituximab IV infusion once every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Measured Values

	Rituximab	Obinutuzumab
Number of Participants Analyzed	86	87

	Rituximab	Obinutuzumab
Number of Participants With Infusion Related Reactions [units: Participants]	44	70

23. Secondary Outcome Measure:

Measure Title	Number of Participants With Human Anti-Chimeric Antibodies (HACA)
Measure Description	Blood was collected on Day 1 and was sent to a central laboratory for analysis of human anti-chimeric antibodies (anti-rituximab antibodies) using a validated enzyme-linked immunosorbent assay (ELISA). HACA samples were not collected for participants randomized to the rituximab arm.
Time Frame	Day 1
Safety Issue?	No

Analysis Population Description

Participants from the Safety Population, all randomized participants who received study drug, who had samples available for HACA analysis.

Reporting Groups

	Description
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Measured Values

	Obinutuzumab
Number of Participants Analyzed	86
Number of Participants With Human Anti-Chimeric Antibodies (HACA) [units: Participants]	1

24. Secondary Outcome Measure:

Measure Title	Number of Participants With Human Anti-Human Antibodies (HAHA)

Measure Description	Blood was collected on Day 1 pre-infusion, during the safety follow-up for those patients who did not enter the Extension period and 6 months after the last infusion of the Extension Period if applicable. Blood was sent to a central laboratory and was tested for anti-obinutuzumab antibodies using a validated enzyme-linked immunosorbent assay (ELISA). HAHA samples were not collected for participants randomized to the rituximab arm.
Time Frame	Randomization to Clinical cutoff: 07 March 2013 (Up to 43.2 months)
Safety Issue?	No

Analysis Population Description

Safety Population included all randomized participants who received study drug.

Reporting Groups

	Description
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Measured Values

	Obinutuzumab
Number of Participants Analyzed	86
Number of Participants With Human Anti-Human Antibodies (HAHA) [units: Participants]	0

Reported Adverse Events

Time Frame	First dose of study drug to 28 days past last dose of study drug (Up to 27 Months)
Additional Description	Safety population included all randomized patients who received at least one dose of study drug. Serious Adverse Events that occurred during treatment are reported.

Reporting Groups

	Description
Rituximab	Participants received 375 mg/m^2 rituximab IV infusion once a week on Days 1, 8, 15 and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression were eligible to receive a 375 mg/m^2 rituximab IV infusion once every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.
Obinutuzumab	Participants received 1000 mg obinutuzumab intravenous (IV) infusion once a week on Days 1, 8, 15, and 22 in the Induction Period. 2 months following the last infusion, participants without disease progression, were eligible to receive a 1000 mg IV infusion every two months for 2 years in the Extension Period. All participants received oral acetaminophen/ paracetamol (1000 mg) and an antihistamine such as diphenhydramine (50-100 mg), 30-60 minutes prior to each infusion.

Serious Adverse Events

	Rituximab	Obinutuzumab
	Affected/At Risk (%)	Affected/At Risk (%)
Total	13/86 (15.12%)	13/87 (14.94%)
Blood and lymphatic system disorders		
Eosinophilia [A] †	0/86 (0%)	1/87 (1.15%)
Febrile neutropenia [A] †	2/86 (2.33%)	2/87 (2.3%)
Neutropenia [A] †	1/86 (1.16%)	0/87 (0%)
Cardiac disorders		
Angina pectoris [A] †	0/86 (0%)	1/87 (1.15%)
Cardio-respiratory arrest [A] †	1/86 (1.16%)	0/87 (0%)
Diastolic dysfunction [A] †	0/86 (0%)	1/87 (1.15%)
General disorders		
Pyrexia [A] †	0/86 (0%)	1/87 (1.15%)
Hepatobiliary disorders		
Hepatitis cholestatic [A] †	1/86 (1.16%)	0/87 (0%)
Infections and infestations		
Cellulitis [A] †	1/86 (1.16%)	0/87 (0%)

	Rituximab	Obinutuzumab
	Affected/At Risk (%)	Affected/At Risk (%)
Chronic sinusitis [A] †	0/86 (0%)	1/87 (1.15%)
Herpes zoster disseminated [A] †	0/86 (0%)	1/87 (1.15%)
Pneumonia [A] †	2/86 (2.33%)	2/87 (2.3%)
Respiratory tract infection [A] †	1/86 (1.16%)	0/87 (0%)
Injury, poisoning and procedural complications		
Fibula fracture [A] †	1/86 (1.16%)	0/87 (0%)
Infusion related reaction [A] †	1/86 (1.16%)	2/87 (2.3%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Ovarian cancer [A] †	1/86 (1.16%)	0/87 (0%)
Psychiatric disorders		
Confusional state [A] †	1/86 (1.16%)	0/87 (0%)
Renal and urinary disorders		
Renal colic [A] †	0/86 (0%)	1/87 (1.15%)
Respiratory, thoracic and mediastinal disorders		
Bronchiectasis [A] †	0/86 (0%)	1/87 (1.15%)
Cough [A] †	0/86 (0%)	1/87 (1.15%)
Dyspnoea [A] †	1/86 (1.16%)	0/87 (0%)
Pleural effusion [A] †	0/86 (0%)	1/87 (1.15%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 16.0

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Rituximab	Obinutuzumab
	Affected/At Risk (%)	Affected/At Risk (%)
Total	70/86 (81.4%)	79/87 (90.8%)
Blood and lymphatic system disorders		
Neutropenia [A] †	6/86 (6.98%)	3/87 (3.45%)
Gastrointestinal disorders		
Abdominal pain upper [A] †	6/86 (6.98%)	2/87 (2.3%)
Diarrhoea [A] †	7/86 (8.14%)	7/87 (8.05%)
Nausea [A] †	7/86 (8.14%)	8/87 (9.2%)
Vomiting [A] †	3/86 (3.49%)	4/87 (4.6%)
General disorders		
Asthenia [A] †	5/86 (5.81%)	6/87 (6.9%)
Fatigue [A] †	17/86 (19.77%)	23/87 (26.44%)
Oedema peripheral [A] †	4/86 (4.65%)	6/87 (6.9%)
Pyrexia [A] †	9/86 (10.47%)	5/87 (5.75%)
Infections and infestations		
Bronchitis [A] †	3/86 (3.49%)	7/87 (8.05%)
Herpes zoster [A] †	2/86 (2.33%)	4/87 (4.6%)
Influenza [A] †	5/86 (5.81%)	3/87 (3.45%)
Nasopharyngitis [A] †	4/86 (4.65%)	6/87 (6.9%)
Rhinitis [A] †	4/86 (4.65%)	4/87 (4.6%)
Sinusitis [A] †	4/86 (4.65%)	6/87 (6.9%)
Upper respiratory tract infection [A] †	9/86 (10.47%)	9/87 (10.34%)
Injury, poisoning and procedural complications		

	Rituximab	Obinutuzumab
	Affected/At Risk (%)	Affected/At Risk (%)
Infusion related reactions [A] †	43/86 (50%)	62/87 (71.26%)
Metabolism and nutrition disorders		
Decreased appetite [A] †	3/86 (3.49%)	8/87 (9.2%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] †	8/86 (9.3%)	4/87 (4.6%)
Back pain [A] †	3/86 (3.49%)	7/87 (8.05%)
Myalgia [A] †	2/86 (2.33%)	5/87 (5.75%)
Nervous system disorders		
Dizziness [A] †	6/86 (6.98%)	4/87 (4.6%)
Headache [A] †	7/86 (8.14%)	8/87 (9.2%)
Paraesthesia [A] †	2/86 (2.33%)	5/87 (5.75%)
Psychiatric disorders		
Insomnia [A] †	1/86 (1.16%)	4/87 (4.6%)
Respiratory, thoracic and mediastinal disorders		
Cough [A] †	8/86 (9.3%)	20/87 (22.99%)
Oropharyngeal pain [A] †	5/86 (5.81%)	2/87 (2.3%)
Skin and subcutaneous tissue disorders		
Rash [A] †	3/86 (3.49%)	6/87 (6.9%)
Vascular disorders		
Hypertension [A] †	7/86 (8.14%)	2/87 (2.3%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 16.0

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The Study being conducted under this Agreement is part of the Overall Study. Investigator is free to publish in reputable journals or to present at professional conferences the results of the Study, but only after the first publication or presentation that involves the Overall Study. The Sponsor may request that Confidential Information be deleted and/or the publication be postponed in order to protect the Sponsor's intellectual property rights.

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