



Clinical trial results:

An Open-Label, Multicenter, Randomized, Phase III Study to Investigate the Efficacy and Safety of Bendamustine Compared With Bendamustine + RO5072759 (GA101) in Patients With Rituximab-Refractory, Indolent Non-Hodgkin's Lymphoma

Summary

EudraCT number	2009-015504-25
Trial protocol	CZ BE AT DE FR IT GB ES SE NL
Global end of trial date	

Results information

Result version number	v1
This version publication date	12 October 2016
First version publication date	12 October 2016

Trial information

Trial identification

Sponsor protocol code	GO01297
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01059630
WHO universal trial number (UTN)	-
Other trial identifiers	Genentech Study ID: GAO4753g

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	01 September 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 September 2014
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

This is a Phase III, open-label, multicenter, randomized study to investigate the efficacy and safety of obinutuzumab (RO5072759, GA101) combined with bendamustine compared with bendamustine alone in participants with rituximab-refractory, Indolent non-Hodgkin lymphoma (iNHL).

Protection of trial subjects:

This study was conducted in accordance with the United States Food and Drug Administration (USFDA) regulations, the International Conference on Harmonisation (ICH) E6 Guideline for Good Clinical Practice, and applicable local, state, and federal laws, as well as other applicable country laws.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 April 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	48 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 5
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	Canada: 95
Country: Number of subjects enrolled	Czech Republic: 30
Country: Number of subjects enrolled	France: 78
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Italy: 16
Country: Number of subjects enrolled	Netherlands: 17
Country: Number of subjects enrolled	Russian Federation: 22
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	Sweden: 13
Country: Number of subjects enrolled	Switzerland: 2
Country: Number of subjects enrolled	United Kingdom: 29
Country: Number of subjects enrolled	United States: 69
Worldwide total number of subjects	396
EEA total number of subjects	208

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	220
From 65 to 84 years	172
85 years and over	4

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 469 participants were screened; out of which 73 participants did not meet the inclusion/exclusion criteria.

Period 1

Period 1 title	Induction Period (6 Months)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Bendamustine Alone

Arm description:

Participants received Bendamustine 120 milligrams per meter square (mg/m²) Intravenous (IV) infusion on Days 1 and 2 of each 28-day cycle for up to six cycles.

Arm type	Experimental
Investigational medicinal product name	Bendamustine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received Bendamustine 120 mg/m² IV infusion on Days 1 and 2 of each 28-day cycle for up to six cycles.

Arm title	Obinutuzumab + Bendamustine
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Arm description:

Induction phase: Participants received Bendamustine 90 mg/m² IV on Days 2 and 3 of Cycle 1 and on Days 1 and 2 of Cycles 2-6 (28-day cycles) for the first 10 participants and on Days 1 and 2 of each 28-day cycle for Cycles 1-6 for remaining participants. Participants also received obinutuzumab 1000 mg IV infusion on Days 1, 8, and 15 of Cycle 1; Day 1 of Cycles 2-6.

Maintenance phase: Participants with complete response (CR), partial response (PR) or stable disease (SD) then received obinutuzumab 1000 mg IV infusion every 2 months until disease progression or for up to 2 years (whichever occurred first).

Arm type	Experimental
Investigational medicinal product name	Obinutuzumab
Investigational medicinal product code	
Other name	RO5072759, GA101
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received obinutuzumab 1000 mg IV infusion on Days 1, 8, and 15 of Cycle 1; Day 1 of Cycles 2-6 during induction phase and 1000 mg IV infusion every 2 months until disease progression or for up to 2 years (whichever occurred first) during maintenance phase.

Investigational medicinal product name	Bendamustine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received bendamustine 90 mg/m² IV on Days 2 and 3 of Cycle 1 and on Days 1 and 2 of Cycles 2-6 (28-day cycles) for the first 10 participants and on Days 1 and 2 of each 28-day cycle for Cycles 1-6 for remaining participants.

Number of subjects in period 1	Bendamustine Alone	Obinutuzumab + Bendamustine
Started	202	194
Treated	198	194
Completed	129	156
Not completed	73	38
Consent withdrawn by subject	7	2
Physician decision	2	4
Adverse Event	30	15
Death	2	2
Progressive Disease	14	9
Randomized but not Treated	4	-
Unspecified	1	-
Induction ongoing	13	6

Period 2

Period 2 title	Maintenance Period (up to 2 Years)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Obinutuzumab + Bendamustine
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Arm description:

Induction phase: Participants received Bendamustine 90 mg/m² IV on Days 2 and 3 of Cycle 1 and on Days 1 and 2 of Cycles 2-6 (28-day cycles) for the first 10 participants and on Days 1 and 2 of each 28-day cycle for Cycles 1-6 for remaining participants. Participants also received obinutuzumab 1000 mg IV infusion on Days 1, 8, and 15 of Cycle 1; Day 1 of Cycles 2-6.

Maintenance phase: Participants with complete response (CR), partial response (PR) or stable disease (SD) then received obinutuzumab 1000 mg IV infusion every 2 months until disease progression or for up to 2 years (whichever occurred first).

Arm type	Experimental
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Investigational medicinal product name	Bendamustine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received bendamustine 90 mg/m² IV on Days 2 and 3 of Cycle 1 and on Days 1 and 2 of Cycles 2-6 (28-day cycles) for the first 10 participants and on Days 1 and 2 of each 28-day cycle for Cycles 1-6 for remaining participants.

Investigational medicinal product name	Obinutuzumab
Investigational medicinal product code	
Other name	RO5072759, GA101
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received obinutuzumab 1000 mg IV infusion on Days 1, 8, and 15 of Cycle 1; Day 1 of Cycles 2-6 during induction phase and 1000 mg IV infusion every 2 months until disease progression or for up to 2 years (whichever occurred first) during maintenance phase.

Number of subjects in period 2^[1]	Obinutuzumab + Bendamustine
Started	143
Completed	35
Not completed	108
Maintenance ongoing	46
Consent withdrawn by subject	3
Physician decision	2
Death	2
Progressive Disease	44
Unspecified	3
Adverse Events	8

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Of all participants who completed induction, 13 participants did not start maintenance.

Baseline characteristics

Reporting groups

Reporting group title	Bendamustine Alone
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Reporting group description:

Participants received Bendamustine 120 milligrams per meter square (mg/m²) Intravenous (IV) infusion on Days 1 and 2 of each 28-day cycle for up to six cycles.

Reporting group title	Obinutuzumab + Bendamustine
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Reporting group description:

Induction phase: Participants received Bendamustine 90 mg/m² IV on Days 2 and 3 of Cycle 1 and on Days 1 and 2 of Cycles 2-6 (28-day cycles) for the first 10 participants and on Days 1 and 2 of each 28-day cycle for Cycles 1-6 for remaining participants. Participants also received obinutuzumab 1000 mg IV infusion on Days 1, 8, and 15 of Cycle 1; Day 1 of Cycles 2-6.

Maintenance phase: Participants with complete response (CR), partial response (PR) or stable disease (SD) then received obinutuzumab 1000 mg IV infusion every 2 months until disease progression or for up to 2 years (whichever occurred first).

Reporting group values	Bendamustine Alone	Obinutuzumab + Bendamustine	Total
Number of subjects	202	194	396
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	61.9 ± 11.4	61.9 ± 11.3	-
Gender categorical Units: Subjects			
Female	84	84	168
Male	118	110	228

End points

End points reporting groups

Reporting group title	Bendamustine Alone
Reporting group description: Participants received Bendamustine 120 milligrams per meter square (mg/m ²) Intravenous (IV) infusion on Days 1 and 2 of each 28-day cycle for up to six cycles.	
Reporting group title	Obinutuzumab + Bendamustine
Reporting group description: Induction phase: Participants received Bendamustine 90 mg/m ² IV on Days 2 and 3 of Cycle 1 and on Days 1 and 2 of Cycles 2-6 (28-day cycles) for the first 10 participants and on Days 1 and 2 of each 28-day cycle for Cycles 1-6 for remaining participants. Participants also received obinutuzumab 1000 mg IV infusion on Days 1, 8, and 15 of Cycle 1; Day 1 of Cycles 2-6. Maintenance phase: Participants with complete response (CR), partial response (PR) or stable disease (SD) then received obinutuzumab 1000 mg IV infusion every 2 months until disease progression or for up to 2 years (whichever occurred first).	
Reporting group title	Obinutuzumab + Bendamustine
Reporting group description: Induction phase: Participants received Bendamustine 90 mg/m ² IV on Days 2 and 3 of Cycle 1 and on Days 1 and 2 of Cycles 2-6 (28-day cycles) for the first 10 participants and on Days 1 and 2 of each 28-day cycle for Cycles 1-6 for remaining participants. Participants also received obinutuzumab 1000 mg IV infusion on Days 1, 8, and 15 of Cycle 1; Day 1 of Cycles 2-6. Maintenance phase: Participants with complete response (CR), partial response (PR) or stable disease (SD) then received obinutuzumab 1000 mg IV infusion every 2 months until disease progression or for up to 2 years (whichever occurred first).	

Primary: Number of Participants With Progressive Disease (PD) as Assessed by Independent Review Committee (IRC) or Death

End point title	Number of Participants With Progressive Disease (PD) as Assessed by Independent Review Committee (IRC) or Death ^[1]
End point description: PD was assessed by an IRC according to the modified response criteria for indolent Non-Hodgkin's Lymphoma (iNHL) (Modified Cheson et al, 2007). PD was defined as appearance of any new lesion more than 1.5 centimeters (cm) in any axis during or at the end of therapy, even if other lesions are decreasing in size; at least a 50 percent (%) increase from nadir in the sum of product diameter (SPD) of any previously involved nodes, or in a single involved node, or the size of other lesions (example: splenic or hepatic nodules). To be considered PD, a lymph node with a diameter of the short axis of less than (<) 1.0 cm must increase by greater than or equal to (≥) 50% and to a size of 1.5 multiplied by 1.5 cm or more than 1.5 cm in the long axis; at least a 50% increase in the longest diameter of any single previously identified node greater than (>) 1 cm in its short axis. Intent to treat (ITT) population included all participants who were randomized in the study.	
End point type	Primary
End point timeframe: Baseline until PD or death, whichever occurred first (assessed at baseline, 14 days prior to Cycle [Cy] 4 Day 1 [1 Cy=28days], 28–42 days after Cy 6 Day 1, then every 3 months up to 2 years and every 6 months for next 2 years [up to 4.5 years overall])	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis was planned for this endpoint.

End point values	Bendamustine Alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	194		
Units: participants				
number (not applicable)	104	71		

Statistical analyses

No statistical analyses for this end point

Primary: Progression-Free Survival (PFS) as Assessed by IRC

End point title	Progression-Free Survival (PFS) as Assessed by IRC
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End point description:

PFS: time from randomization to first occurrence of PD or death as assessed by IRC according to modified response criteria for iNHL (modified Cheson et al, 2007). PD: appearance of any new lesion more than 1.5 cm in any axis during or at end of therapy, even if other lesions decrease in size; at least 50% increase from nadir in SPD of any previously involved nodes, or in single involved node, or size of other lesions (e.g., splenic or hepatic nodules). To be PD, lymph node with diameter of short axis of <1.0 cm must increase by $\geq 50\%$ and to size of 1.5 multiplied by 1.5 cm or more than 1.5 cm in long axis; at least 50% increase in longest diameter of any single previously identified node >1 cm in its short axis. PFS was estimated using Kaplan-Meier method and 95% confidence interval (CI) for median was computed using method of Brookmeyer and Crowley. ITT population. The number 99999 signified data could not be estimated due to higher (>50%) number of censored participants.

End point type	Primary
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End point timeframe:

Baseline until PD or death, whichever occurred first (assessed at baseline, 14 days prior to Cy 4 Day 1 [1 Cy=28days], 28–42 days after Cy 6 Day 1, then every 3 months up to 2 years and every 6 months for next 2 years [up to 4.5 years overall])

End point values	Bendamustine Alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	194		
Units: months				
median (confidence interval 95%)	14.9 (12.8 to 16.6)	99999 (22.5 to 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

Randomization was stratified for iNHL subtype (follicular versus other), refractory type (rituximab monotherapy versus rituximab + chemotherapy), number of prior therapies (less than or equal to 2 versus greater than 2) and geographic region.

Comparison groups	Bendamustine Alone v Obinutuzumab + Bendamustine
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Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	0.74

Secondary: Number of Participants With PD or Death as Assessed by Investigator

End point title	Number of Participants With PD or Death as Assessed by Investigator
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End point description:

PD was assessed by an investigator according to the modified response criteria for iNHL (modified Cheson et al, 2007). PD was defined as appearance of any new lesion more than 1.5 cm in any axis during or at the end of therapy, even if other lesions are decreasing in size; at least a 50% increase from nadir in the SPD of any previously involved nodes, or in a single involved node, or the size of other lesions (e.g., splenic or hepatic nodules). To be considered PD, a lymph node with a diameter of the short axis of <1.0 cm must increase by $\geq 50\%$ and to a size of 1.5 multiplied by 1.5 cm or more than 1.5 cm in the long axis; at least a 50% increase in the longest diameter of any single previously identified node >1 cm in its short axis. ITT population.

End point type	Secondary
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End point timeframe:

Baseline until PD or death, whichever occurred first (assessed at baseline, 14 days prior to Cy 4 Day 1 [1 Cy=28days], 28–42 days after Cy 6 Day 1, then every 3 months up to 2 years and every 6 months for next 2 years [up to 4.5 years overall])

End point values	Bendamustine Alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	194		
Units: participants				
number (not applicable)	115	77		

Statistical analyses

No statistical analyses for this end point

Secondary: PFS as Assessed by Investigator

End point title	PFS as Assessed by Investigator
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End point description:

PFS: time from randomization to first occurrence of PD as assessed by investigator according to

modified response criteria for iNHL (Modified Cheson et al, 2007), or death from any cause on study. PD: appearance of any new lesion more than 1.5 cm in any axis during/at end of therapy, even if other lesions decreases in size; at least 50% increase from nadir in SPD of any previously involved nodes, or in single involved node, or size of other lesions. To be considered PD, lymph node with diameter of the short axis of <1.0 cm must increase by $\geq 50\%$ and to a size of 1.5 multiplied by 1.5 cm or more than 1.5 cm in the long axis; at least 50% increase in the longest diameter of any single previously identified node >1 cm in its short axis. PFS was estimated using Kaplan-Meier method and 95% CI for median was computed using method of Brookmeyer and Crowley. ITT population. The number 99999 signified data could not be estimated due to higher (>50%) number of censored participants.

End point type	Secondary
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End point timeframe:

Baseline until PD or death, whichever occurred first (assessed at baseline, 14 days prior to Cy 4 Day 1 [1 Cy=28days], 28–42 days after Cy 6 Day 1, then every 3 months up to 2 years and every 6 months for next 2 years [up to 4.5 years overall])

End point values	Bendamustine Alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	194		
Units: Months				
median (confidence interval 95%)	14 (11.7 to 16)	29.2 (20.2 to 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

Randomization was stratified for iNHL subtype (follicular versus other), refractory type (rituximab monotherapy versus rituximab + chemotherapy), number of prior therapies (less than or equal to 2 versus greater than 2) and geographic region.

Comparison groups	Bendamustine Alone v Obinutuzumab + Bendamustine
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	0.7

Secondary: Percentage of Participants With Objective Response as Assessed by IRC and Investigator

End point title	Percentage of Participants With Objective Response as Assessed by IRC and Investigator
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End point description:

Objective response was defined as having CR or PR as assessed according to the modified response criteria for iNHL (Modified Cheson et al, 2007). CR: Complete disappearance of all detectable clinical evidence of disease and disease-related symptoms if present prior to therapy, liver and spleen have returned to normal size (if enlarged at baseline), If the bone marrow was involved by lymphoma prior to treatment, the infiltrate must have cleared on repeat bone marrow biopsy. PR: at least 50% regression of measurable disease compared to tumors measured by a baseline scan and no new sites; no increase in the size of the other nodes, liver, or spleen; with the exception of splenic and hepatic nodules, involvement of other organs is usually assessable and no measurable disease should be present. ITT population. Here, number of participants analyzed signified those participants who had at least one post-baseline assessment.

End point type	Secondary
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End point timeframe:

Baseline until PD or death, whichever occurred first (assessed at baseline, 14 days prior to Cy 4 Day 1 [1 Cy=28days], 28–42 days after Cy 6 Day 1, then every 3 months up to 12 months overall)

End point values	Bendamustine Alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	192		
Units: percentage of participants				
number (confidence interval 95%)				
IRC Assessment	76.6 (70.11 to 82.37)	78.6 (72.17 to 84.22)		
Investigator Assessment	82.2 (76.17 to 87.3)	82.8 (76.72 to 87.86)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

Statistical Analysis 1 for Percentage of Participants With Objective Response as Assessed by IRC.

Comparison groups	Bendamustine Alone v Obinutuzumab + Bendamustine
Number of subjects included in analysis	389
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.743
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in response rate
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.56
upper limit	10.55

Statistical analysis title	Statistical Analysis 2
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Statistical analysis description:

Statistical Analysis 2 for Percentage of Participants With Objective Response as Assessed by Investigator.

Comparison groups	Bendamustine Alone v Obinutuzumab + Bendamustine
Number of subjects included in analysis	389
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8946
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in response rate
Point estimate	0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.25
upper limit	8.41

Secondary: Percentage of Participants With Best Overall Response (BOR) as Assessed by IRC and Investigator

End point title	Percentage of Participants With Best Overall Response (BOR) as Assessed by IRC and Investigator
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End point description:

BOR: best response for a participant, observed during assessment period according to modified response criteria for iNHL (Modified Cheson et al, 2007). CR: complete disappearance of all detectable clinical evidence of disease and disease-related symptoms if present prior to therapy, PR: at least 50% regression of measurable disease compared to tumors measured by baseline scan and no new sites; no increase in size of the other nodes, liver, or spleen; SD: Failing to attain the criteria needed for a CR or PR, but not fulfilling those for PD, PD: appearance of any new lesion more than 1.5 cm in any axis during or at end of therapy, even if other lesions are decreasing in size; at least a 50% increase from nadir in SPD of any previously involved nodes, or in single involved node, or size of other lesions. ITT population. Here, number of participants analyzed signified those participants who had at least one post-baseline assessment.

End point type	Secondary
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End point timeframe:

Baseline until PD or death, whichever occurred first (assessed at baseline, 14 days prior to Cy 4 Day 1 [1 Cy=28days], 28–42 days after Cy 6 Day 1, then every 3 months up to 12 months overall)

End point values	Bendamustine Alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	192		
Units: percentage of participants				
number (confidence interval 95%)				
IRC Assessment: CR	17.3 (12.26 to 23.27)	16.7 (11.69 to 22.71)		
IRC Assessment: PR	59.4 (52.18 to 66.31)	62 (54.71 to 68.87)		
IRC Assessment: SD	11.7 (7.55 to 17)	10.9 (6.9 to 16.23)		
IRC Assessment: PD	4.1 (1.77 to 7.84)	4.7 (2.17 to 8.71)		

IRC Assessment: Unable to evaluate	0.5 (0.01 to 2.8)	1 (0.13 to 3.71)		
IRC Assessment: Missing	7.1 (3.94 to 11.64)	4.7 (2.17 to 8.71)		
Investigator Assessment: CR	21.3 (15.82 to 27.71)	22.4 (16.71 to 28.96)		
Investigator Assessment: PR	60.9 (53.72 to 67.77)	60.4 (53.12 to 67.38)		
Investigator Assessment: SD	6.6 (3.56 to 11.02)	6.8 (3.65 to 11.3)		
Investigator Assessment: PD	3.6 (1.44 to 7.18)	5.7 (2.89 to 10.02)		
Investigator Assessment: Unable to evaluate	1.5 (0.32 to 4.39)	0.5 (0.01 to 2.87)		
Investigator Assessment: Missing	6.1 (3.19 to 10.4)	4.2 (1.82 to 8.04)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Objective Response at the End of Induction Treatment as Assessed by IRC and Investigator

End point title	Percentage of Participants With Objective Response at the End of Induction Treatment as Assessed by IRC and Investigator
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End point description:

Objective response was defined as having CR or PR as assessed according to the modified response criteria for iNHL (Modified Cheson et al, 2007). CR: Complete disappearance of all detectable clinical evidence of disease and disease-related symptoms if present prior to therapy, liver and spleen have returned to normal size (if enlarged at baseline), If the bone marrow was involved by lymphoma prior to treatment, the infiltrate must have cleared on repeat bone marrow biopsy. PR: at least 50% regression of measurable disease compared to tumors measured by a baseline scan and no new sites; no increase in the size of the other nodes, liver, or spleen; with the exception of splenic and hepatic nodules, involvement of other organs is usually assessable and no measurable disease should be present. ITT population. Here, number of participants analyzed signified those participants who had reached the end of induction treatment response assessment.

End point type	Secondary
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End point timeframe:

Baseline until end of induction treatment (assessed at baseline, 14 days prior to Cy 4 Day 1 [1 Cy=28days], 28–42 days after Cy 6 Day 1)

End point values	Bendamustine Alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	188		
Units: percentage of participants				
number (confidence interval 95%)				
IRC Assessment	63 (55.65 to 69.86)	69.1 (62.02 to 75.67)		
Investigator Assessment	67.7 (60.56 to 74.33)	76.6 (69.88 to 82.45)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Statistical Analysis 1 for Percentage of Participants With Objective Response at the End of Induction Treatment as Assessed by IRC.	
Comparison groups	Bendamustine Alone v Obinutuzumab + Bendamustine
Number of subjects included in analysis	377
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3062
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in response rate
Point estimate	6.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.64
upper limit	16.02

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Statistical Analysis 2 for Percentage of Participants With Objective Response at the End of Induction Treatment as Assessed by Investigator.	
Comparison groups	Bendamustine Alone v Obinutuzumab + Bendamustine
Number of subjects included in analysis	377
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0506
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in response rate
Point estimate	8.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	18.16

Secondary: Percentage of Participants With BOR at the End of Induction Treatment as Assessed by IRC and Investigator

End point title	Percentage of Participants With BOR at the End of Induction
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End point description:

BOR: best response for a participant, observed during assessment period according to modified response criteria for iNHL (Modified Cheson et al, 2007). CR: complete disappearance of all detectable clinical evidence of disease and disease-related symptoms if present prior to therapy, PR: at least 50% regression of measurable disease compared to tumors measured by baseline scan and no new sites; no increase in size of the other nodes, liver, or spleen; SD: Failing to attain the criteria needed for a CR or PR, but not fulfilling those for PD, PD: appearance of any new lesion more than 1.5 cm in any axis during or at end of therapy, even if other lesions are decreasing in size; at least a 50% increase from nadir in SPD of any previously involved nodes, or in single involved node, or size of other lesions. ITT population. Here, number of participants analyzed signified those participants who had reached the end of induction treatment response assessment.

End point type	Secondary
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End point timeframe:

Baseline until end of induction treatment (assessed at baseline, 14 days prior to Cy 4 Day 1 [1 Cy=28days], 28–42 days after Cy 6 Day 1)

End point values	Bendamustine Alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	188		
Units: percentage of participants				
number (confidence interval 95%)				
IRC Assessment: CR	12.2 (7.87 to 17.7)	11.2 (7.05 to 16.57)		
IRC Assessment: PR	50.8 (43.44 to 58.12)	58 (50.58 to 65.12)		
IRC Assessment: SD	9.5 (5.74 to 14.63)	10.1 (6.2 to 15.33)		
IRC Assessment: PD	9 (5.33 to 14.01)	9 (5.36 to 14.08)		
IRC Assessment: Unable to Evaluate	2.6 (0.86 to 6.07)	2.1 (0.58 to 5.36)		
IRC Assessment: Missing	15.9 (10.97 to 21.88)	9.6 (5.77 to 14.71)		
Investigator Assessment: CR	15.9 (10.97 to 21.88)	16.5 (11.49 to 22.58)		
Investigator Assessment: PR	51.9 (44.48 to 59.16)	60.1 (52.73 to 67.16)		
Investigator Assessment: SD	3.2 (1.17 to 6.78)	4.3 (1.85 to 8.21)		
Investigator Assessment: PD	11.1 (7.01 to 16.48)	9 (5.36 to 14.08)		
Investigator Assessment: Unable to Evaluate	3.2 (1.17 to 6.78)	0.5 (0.01 to 2.93)		
Investigator Assessment: Missing	14.8 (10.08 to 20.69)	9.6 (5.77 to 14.71)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR) as Assessed by IRC

End point title	Duration of Response (DoR) as Assessed by IRC
End point description:	
DoR: time from first objective response of CR/PR to first occurrence of PD/relapse/death from any cause. CR: Complete disappearance of all detectable clinical evidence of disease and disease-related symptoms if present prior to therapy; liver, spleen returned to normal size (if enlarged at baseline); if bone marrow was involved by lymphoma prior to treatment, infiltrate must have cleared on repeat bone marrow biopsy. PR: at least 50% regression of measurable disease compared to baseline scan and no new sites; no increase in size of other nodes, liver, or spleen; with exception of splenic, hepatic nodules; involvement of other organs is usually assessable; no presence of measurable disease. PD: appearance of any new lesion >1.5 cm in any axis during or at end of therapy, even if other lesions are decreasing in size; at least 50% increase from nadir in SPD of any previously involved nodes, or in single involved node, or size of other lesions. DoR was estimated using Kaplan-Meier method.	
End point type	Secondary
End point timeframe:	
Baseline until PD or death, whichever occurred first (assessed at baseline, 14 days prior to Cy 4 Day 1 [1 Cy=28days], 28–42 days after Cy 6 Day 1, then every 3 months up to 2 years and every 6 months for next 2 years [up to 4.5 years overall])	

End point values	Bendamustine Alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	154		
Units: months				
median (confidence interval 95%)	13.2 (11 to 14.1)	99999 (25.4 to 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Randomization was stratified for iNHL subtype (follicular versus other), refractory type (rituximab monotherapy versus rituximab + chemotherapy), number of prior therapies (less than or equal to 2 versus greater than 2) and geographic region.	
Comparison groups	Bendamustine Alone v Obinutuzumab + Bendamustine
Number of subjects included in analysis	308
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	0.61

Secondary: Disease-Free Survival (DFS) in Participants With CR as Assessed by IRC

End point title	Disease-Free Survival (DFS) in Participants With CR as Assessed by IRC
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End point description:

DFS: time from first occurrence of documented CR until progression on basis of IRC assessments (as per modified response criteria for iNHL [Modified Cheson et al, 2007]) or death from any cause on study.
 CR: Complete disappearance of all detectable clinical evidence of disease and disease-related symptoms, liver and spleen returned to normal size if enlarged at baseline, If bone marrow was involved by lymphoma prior to treatment, infiltrate must have cleared on repeat bone marrow biopsy. PD: appearance of any new lesion >1.5 cm in any axis during/at end of therapy, even if other lesions decreases in size; at least 50% increase from nadir in SPD of any previously involved nodes, or in single involved node, or size of other lesions. DFS was estimated using Kaplan-Meier method. ITT population. Number of participants analyzed signified participants who had an objective response of CR. Number 99999 signified data could not be estimated due to higher (>50%) number of censored participants.

End point type	Secondary
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End point timeframe:

Baseline until PD or death, whichever occurred first (assessed at baseline, 14 days prior to Cy 4 Day 1 [1 Cy=28days], 28–42 days after Cy 6 Day 1, then every 3 months up to 2 years and every 6 months for next 2 years [up to 4.5 years overall])

End point values	Bendamustine Alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	42		
Units: months				
median (confidence interval 95%)	13.2 (8.2 to 99999)	99999 (99999 to 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

Randomization was stratified for iNHL subtype (follicular versus other), refractory type (rituximab monotherapy versus rituximab + chemotherapy), number of prior therapies (less than or equal to 2 versus greater than 2) and geographic region.

Comparison groups	Bendamustine Alone v Obinutuzumab + Bendamustine
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	0.4

Secondary: Event-free Survival (EFS) as Assessed by IRC

End point title	Event-free Survival (EFS) as Assessed by IRC
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End point description:

EFS was defined as the time between the date of randomization and the date of PD/relapse based on IRC assessments (as per modified response criteria for iNHL [Modified Cheson et al, 2007]), death from any cause on study, or start of a new anti-lymphoma therapy. PD: appearance of any new lesion >1.5 cm in any axis during or at end of therapy, even if other lesions are decreasing in size; at least a 50% increase from nadir in SPD of any previously involved nodes, or in a single involved node, or size of other lesions. EFS was estimated using Kaplan-Meier method. ITT population. The number 99999 signified data could not be estimated due to higher (>50%) number of censored participants.

End point type	Secondary
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End point timeframe:

Baseline until PD or death, whichever occurred first (assessed at baseline, 14 days prior to Cy 4 Day 1 [1 Cy=28days], 28–42 days after Cy 6 Day 1, then every 3 months up to 2 years and every 6 months for next 2 years [up to 4.5 years overall])

End point values	Bendamustine Alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	194		
Units: months				
median (confidence interval 95%)	13.7 (11.4 to 16.2)	26.8 (14.1 to 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

Randomization was stratified for iNHL subtype (follicular versus other), refractory type (rituximab monotherapy versus rituximab + chemotherapy), number of prior therapies (less than or equal to 2 versus greater than 2) and geographic region.

Comparison groups	Bendamustine Alone v Obinutuzumab + Bendamustine
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	0.76

Secondary: Percentage of Participants Who Died

End point title	Percentage of Participants Who Died
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End point description:

ITT population.

End point type	Secondary
End point timeframe:	
Baseline until death (up to 4.5 years overall)	

End point values	Bendamustine Alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	194		
Units: percentage of participants				
number (not applicable)	20.3	17.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	
OS was defined as the time between the date of randomization and the date of death from any cause. OS was estimated using Kaplan-Meier method and 95% CI for median was computed using the method of Brookmeyer and Crowley. ITT population. The number 99999 signified data could not be estimated due to higher (>50%) number of censored participants.	
End point type	Secondary
End point timeframe:	
Baseline until death (up to 4.5 years overall)	

End point values	Bendamustine Alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	194		
Units: months				
median (confidence interval 95%)	99999 (39.8 to 99999)	99999 (99999 to 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Randomization was stratified for iNHL subtype (follicular versus other), refractory type (rituximab monotherapy versus rituximab + chemotherapy), number of prior therapies (less than or equal to 2 versus greater than 2) and geographic region.	

Comparison groups	Bendamustine Alone v Obinutuzumab + Bendamustine
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4017
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	1.3

Secondary: Change From Baseline (CFB) in Functional Assessment of Cancer Therapy-Lymphoma (FACT-Lym)-Physical Well Being Sub-scale Score

End point title	Change From Baseline (CFB) in Functional Assessment of Cancer Therapy-Lymphoma (FACT-Lym)-Physical Well Being Sub-scale Score
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End point description:

FACT-Lym measures 5 sub-scales which includes 42 items; responses to each item range from 0 (Not at all) to 4 (Very much). Total score range: 0-168. Physical well-being sub-scale includes 7 items measured on 0-4 point scale; total score ranges from 0-28. Higher scores indicates better participant-reported outcome (PRO)/quality of life (QoL). In timeframe, follow-up months represents months after end of induction (e.g. Follow-up Month 2 is 2 months after end of induction); extension follow-up months represents months after end of 2 years normal follow-up (e.g. extension follow-up Month 6 is 6 months after end of normal 2 year follow-up). ITT population. Here, number of participants analyzed signified those participants who were evaluable for this outcome and "n" signified those participants who were evaluable for a specified time point. The number 99999 signified data not available either because no participant or only one participant was evaluable.

End point type	Secondary
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End point timeframe:

Baseline, Day 1 of Cycles 1, 3, 4, 5, End of induction treatment (up to Month 6); Follow-up Months 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, Final Follow-up (up to 2 years after end of induction); Extension follow-up Months 6 and 18

End point values	Bendamustine Alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	177		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=181, 177)	22.63 (± 5.16)	22.72 (± 4.65)		
CFB at Cycle 1 Day 1 (n=0, 0)	99999 (± 99999)	99999 (± 99999)		
CFB at Cycle 3 Day 1 (n=146, 147)	-1.78 (± 5.47)	-0.77 (± 4.13)		
CFB at Cycle 4 Day 1 (n=5, 2)	-6.8 (± 4.21)	-3 (± 2.83)		
CFB at Cycle 5 Day 1 (n=130, 137)	-1.99 (± 5.07)	-0.77 (± 4.22)		
CFB at End of Induction Treatment (n=132, 135)	-0.96 (± 5.23)	-0.63 (± 4.71)		

CFB at Follow-up Month 2 (n=91, 119)	0.42 (± 5.21)	0.57 (± 4.46)		
CFB at Follow-up Month 4 (n= 80, 108)	0.36 (± 4.44)	0.84 (± 4.32)		
CFB at Follow-up Month 6 (n= 67, 94)	0.31 (± 3.74)	0.77 (± 3.62)		
CFB at Follow-up Month 8 (n= 62, 86)	-0.12 (± 3.42)	0.78 (± 3.82)		
CFB at Follow-up Month 10 (n= 47, 71)	-0.28 (± 4.42)	0.47 (± 4.01)		
CFB at Follow-up Month 12 (n= 38, 70)	0.5 (± 4.26)	0.66 (± 4.6)		
CFB at Follow-up Month 14 (n= 32, 62)	0.14 (± 4.24)	0.5 (± 4)		
CFB at Follow-up Month 16 (n= 26, 59)	-0.47 (± 3.36)	0.86 (± 3.62)		
CFB at Follow-up Month 18 (n= 23, 50)	-0.22 (± 4.03)	0.6 (± 4.27)		
CFB at Follow-up Month 20 (n= 22, 41)	-0.31 (± 3.96)	0.35 (± 4.23)		
CFB at Follow-up Month 22 (n=16, 38)	-0.73 (± 4.06)	-0.15 (± 5.32)		
CFB at Follow-up Month 24 (n=15, 33)	-1.23 (± 3.81)	0.35 (± 5.42)		
CFB at Final Follow-up (n=59, 58)	-0.09 (± 4.15)	0.12 (± 5.17)		
CFB at Extension Follow-up Month 6 (n= 7, 18)	0.31 (± 2.6)	1.09 (± 5.33)		
CFB at Extension Follow-up Month 18 (n= 1, 1)	1 (± 99999)	7 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: CFB in FACT-Lym-Social/Family Well-being Sub-scale Score

End point title	CFB in FACT-Lym-Social/Family Well-being Sub-scale Score
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End point description:

FACT-Lym measures 5 sub-scales which includes 42 items; responses to each item range from 0 (Not at all) to 4 (Very much). Total score range: 0-168. Social/family well-being sub-scale includes 7 items measured on 0-4 point scale; total score ranges from 0-28. Higher scores indicates better PRO/QoL. In timeframe, follow-up months represents months after end of induction (e.g. Follow-up Month 2 is 2 months after end of induction); extension follow-up months represents months after end of 2 years normal follow-up (e.g. extension follow-up Month 6 is 6 months after end of normal 2 year follow-up). ITT population. Here, number of participants analyzed signified those participants who were evaluable for this outcome and "n" signified those participants who were evaluable for a specified time point. The number 99999 signified data not available either because no participant or only one participant was evaluable.

End point type	Secondary
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End point timeframe:

Baseline, Day 1 of Cycles 1, 3, 4, 5, End of induction treatment (up to Month 6); Follow-up Months 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, Final Follow-up (up to 2 years after end of induction); Extension follow-up Months 6 and 18

End point values	Bendamustine Alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	180	181		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=180, 181)	22.14 (± 5.58)	22.17 (± 5.48)		
CFB at Cycle 1 Day 1 (n=0, 0)	99999 (± 99999)	99999 (± 99999)		

CFB at Cycle 3 Day 1 (n=145, 151)	-0.35 (± 3.39)	-0.1 (± 3.94)		
CFB at Cycle 4 Day 1 (n=5, 3)	-1 (± 3.67)	3.11 (± 2.83)		
CFB at Cycle 5 Day 1 (n=129, 141)	-0.82 (± 3.45)	-0.39 (± 4.4)		
CFB at End of Induction Treatment (n=131, 138)	-1.06 (± 4.69)	-0.91 (± 3.62)		
CFB at Follow-up Month 2 (n=90, 123)	-0.48 (± 3.89)	-0.59 (± 5.54)		
CFB at Follow-up Month 4 (n=80, 111)	0.09 (± 3.76)	-0.26 (± 5.2)		
CFB at Follow-up Month 6 (n=67, 95)	-0.14 (± 2.84)	-0.07 (± 4.81)		
CFB at Follow-up Month 8 (n=62, 88)	-0.48 (± 3.48)	-0.47 (± 5.19)		
CFB at Follow-up Month 10 (n=47, 73)	0.05 (± 3.45)	0.16 (± 5.38)		
CFB at Follow-up Month 12 (n=38, 72)	0.13 (± 2.31)	-0.14 (± 5.53)		
CFB at Follow-up Month 14 (n=32, 64)	0.82 (± 3.32)	-0.17 (± 3.86)		
CFB at Follow-up Month 16 (n=26, 61)	0.41 (± 3.68)	0.4 (± 5.63)		
CFB at Follow-up Month 18 (n=23, 51)	0.3 (± 3.89)	0.49 (± 6.02)		
CFB at Follow-up Month 20 (n=22, 43)	-0.82 (± 4.61)	0.82 (± 6.14)		
CFB at Follow-up Month 22 (n=16, 40)	-0.97 (± 5.47)	-0.39 (± 5.41)		
CFB at Follow-up Month 24 (n=15, 34)	-0.97 (± 2.56)	0.23 (± 4.32)		
CFB at Final Follow-up (n=59, 59)	-0.47 (± 3.34)	-0.3 (± 5.36)		
CFB at Extension Follow-up Month 6 (n=7, 18)	-0.64 (± 2.68)	0.62 (± 4.01)		
CFB at Extension Follow-up Month 18 (n=1, 1)	-1 (± 99999)	10 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: CFB in FACT-Lym-Emotional Well Being Sub-scale Score

End point title	CFB in FACT-Lym-Emotional Well Being Sub-scale Score
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End point description:

FACT-Lym measures 5 sub-scales which includes 42 items; responses to each item range from 0 (Not at all) to 4 (Very much). Total score range: 0-168. Emotional well-being sub-scale includes 6 items measured on 0-4 point scale; total score ranges from 0-24. Higher scores indicates better PRO/QoL. In timeframe, follow-up months represents months after end of induction (e.g. Follow-up Month 2 is 2 months after end of induction); extension follow-up months represents months after end of 2 years normal follow-up (e.g. extension follow-up Month 6 is 6 months after end of normal 2 year follow-up). ITT population. Here, number of participants analyzed signified those participants who were evaluable for this outcome and "n" signified those participants who were evaluable for a specified time point. The number 99999 signified data not available either because no participant or only one participant was evaluable.

End point type	Secondary
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End point timeframe:

Baseline, Day 1 of Cycles 1, 3, 4, 5, End of induction treatment (up to Month 6); Follow-up Months 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, Final Follow-up (up to 2 years after end of induction); Extension follow-up Months 6 and 18

End point values	Bendamustine Alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	183	184		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=183, 184)	17.43 (± 4.44)	17.73 (± 4.33)		
CFB at Cycle 1 Day 1 (n=0, 0)	99999 (± 99999)	99999 (± 99999)		
CFB at Cycle 3 Day 1 (n=147, 156)	0.54 (± 3.07)	0.75 (± 3.14)		
CFB at Cycle 4 Day 1 (n=5, 3)	-0.6 (± 3.85)	3.4 (± 4.42)		
CFB at Cycle 5 Day 1 (n=131, 144)	0.32 (± 3.11)	0.5 (± 3.59)		
CFB at End of Induction Treatment (n=133, 138)	0.53 (± 3.59)	0.48 (± 3.97)		
CFB at Follow-up Month 2 (n=90, 124)	0.74 (± 4.03)	0.58 (± 3.67)		
CFB at Follow-up Month 4 (n=81, 110)	1.37 (± 3.5)	0.88 (± 3.41)		
CFB at Follow-up Month 6 (n=68, 97)	0.94 (± 3.42)	0.97 (± 3.29)		
CFB at Follow-up Month 8 (n=62, 89)	0.29 (± 3.55)	0.76 (± 3.23)		
CFB at Follow-up Month 10 (n=46, 73)	0.72 (± 3.59)	1.17 (± 2.95)		
CFB at Follow-up Month 12 (n=38, 72)	-0.08 (± 3.98)	0.84 (± 3.01)		
CFB at Follow-up Month 14 (n=32, 64)	0.43 (± 3.48)	0.93 (± 3.58)		
CFB at Follow-up Month 16 (n=26, 62)	0.08 (± 3.77)	0.95 (± 3.49)		
CFB at Follow-up Month 18 (n=22, 52)	0.41 (± 3.1)	0.92 (± 3.01)		
CFB at Follow-up Month 20 (n=22, 44)	-0.14 (± 2.82)	0.84 (± 4.45)		
CFB at Follow-up Month 22 (n=16, 40)	-0.38 (± 2.7)	0.88 (± 3.84)		
CFB at Follow-up Month 24 (n=15, 35)	-0.2 (± 3.19)	0.95 (± 3.76)		
CFB at Final Follow-up (n=58, 61)	0.03 (± 3.85)	0.1 (± 4.9)		
CFB at Extension Follow-up Month 6 (n=7, 18)	-0.43 (± 5.09)	1.21 (± 4.68)		
CFB at Extension Follow-up Month 18 (n=1, 1)	1 (± 99999)	8 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: CFB in FACT-Lym-Functional Well Being Sub-scale Score

End point title	CFB in FACT-Lym-Functional Well Being Sub-scale Score
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End point description:

FACT-Lym measures 5 sub-scales which includes 42 items; responses to each item range from 0 (Not at all) to 4 (Very much). Total score range: 0-168. Functional well-being sub-scale includes 7 items measured on 0-4 point scale; total score ranges from 0-28. Higher scores indicates better PRO/QoL. In timeframe, follow-up months represents months after end of induction (e.g. Follow-up Month 2 is 2 months after end of induction); extension follow-up months represents months after end of 2 years normal follow-up (e.g. extension follow-up Month 6 is 6 months after end of normal 2 year follow-up). ITT population. Here, number of participants analyzed signified those participants who were evaluable for this outcome and "n" signified those participants who were evaluable for a specified time point. The number 99999 signified data not available either because no participant or only one participant was evaluable.

End point type	Secondary
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End point timeframe:

Baseline, Day 1 of Cycles 1, 3, 4, 5, End of induction treatment (up to Month 6); Follow-up Months 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, Final Follow-up (up to 2 years after end of induction); Extension

End point values	Bendamustine Alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	183	186		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=183, 186)	18 ($\pm$ 6.18)	17.84 ($\pm$ 6.07)		
CFB at Cycle 1 Day 1 (n=0, 0)	99999 ($\pm$ 99999)	99999 ($\pm$ 99999)		
CFB at Cycle 3 Day 1 (n=147, 158)	-0.64 ($\pm$ 4.7)	0.39 ($\pm$ 4.74)		
CFB at Cycle 4 Day 1 (n=5, 3)	-0.8 ($\pm$ 2.28)	1.78 ($\pm$ 4.91)		
CFB at Cycle 5 Day 1 (n=131, 146)	-0.88 ($\pm$ 5.04)	0.67 ($\pm$ 5.48)		
CFB at End of Induction Treatment (n=133, 140)	-0.58 ($\pm$ 5.68)	0 ($\pm$ 5.35)		
CFB at Follow-up Month 2 (n=90, 125)	0.32 ($\pm$ 5.54)	0.74 ($\pm$ 5.48)		
CFB at Follow-up Month 4 (n=81, 112)	0.36 ($\pm$ 5.14)	1.3 ($\pm$ 5.77)		
CFB at Follow-up Month 6 (n=67, 97)	0.81 ($\pm$ 4.65)	1.58 ($\pm$ 5.05)		
CFB at Follow-up Month 8 (n=62, 89)	-0.21 ($\pm$ 4.38)	1.03 ($\pm$ 5.75)		
CFB at Follow-up Month 10 (n=47, 74)	1 ($\pm$ 4.42)	1.23 ($\pm$ 5.93)		
CFB at Follow-up Month 12 (n=38, 73)	1.11 ($\pm$ 4.82)	1.96 ($\pm$ 6.63)		
CFB at Follow-up Month 14 (n=32, 64)	1.47 ($\pm$ 4.53)	1.39 ($\pm$ 5.12)		
CFB at Follow-up Month 16 (n=26, 62)	0.89 ($\pm$ 4.17)	2.14 ($\pm$ 6.14)		
CFB at Follow-up Month 18 (n=22, 52)	0.1 ($\pm$ 4.98)	1.87 ($\pm$ 6.77)		
CFB at Follow-up Month 20 (n=22, 44)	-0.81 ($\pm$ 4.55)	1.52 ($\pm$ 7.31)		
CFB at Follow-up Month 22 (n=16, 41)	-1.74 ($\pm$ 4.9)	0.71 ($\pm$ 6.06)		
CFB at Follow-up Month 24 (n=15, 35)	-1.86 ($\pm$ 4.46)	1.5 ($\pm$ 6.84)		
CFB at Final Follow-up (n=58, 63)	-1.03 ($\pm$ 4.95)	0.66 ($\pm$ 7.17)		
CFB at Extension Follow-up Month 6 (n=7, 18)	1.45 ($\pm$ 5.16)	2.61 ($\pm$ 7.46)		
CFB at Extension Follow-up Month 18 (n=1, 1)	-2 ($\pm$ 99999)	0 ($\pm$ 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: CFB in FACT-Lym-Lymphoma Sub-scale Score

End point title	CFB in FACT-Lym-Lymphoma Sub-scale Score
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End point description:

FACT-Lym measures 5 sub-scales which includes 42 items; responses to each item range from 0 (Not at all) to 4 (Very much). Total score range: 0-168. Lymphoma sub-scale includes 15 items measured on 0-4 point scale; total score ranges from 0-60. Higher scores indicates better PRO/QoL. In timeframe, follow-up months represents months after end of induction (e.g. Follow-up Month 2 is 2 months after end of induction); extension follow-up months represents months after end of 2 years normal follow-up (e.g. extension follow-up Month 6 is 6 months after end of normal 2 year follow-up). ITT population. Here, number of participants analyzed signified those participants who were evaluable for this outcome and "n" signified those participants who were evaluable for a specified time point. The number 99999

signified data not available either because no participant or only one participant was evaluable.

End point type	Secondary
End point timeframe:	
Baseline, Day 1 of Cycles 1, 3, 4, 5, End of induction treatment (up to Month 6); Follow-up Months 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, Final Follow-up (up to 2 years after end of induction); Extension follow-up Months 6 and 18	

End point values	Bendamustine Alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	183	144		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=183, 144)	44.88 (± 9.56)	45.55 (± 9.18)		
CFB at Cycle 1 Day 1 (n=0, 0)	99999 (± 99999)	99999 (± 99999)		
CFB at Cycle 3 Day 1 (n=144, 155)	0.68 (± 6.95)	1.05 (± 5.58)		
CFB at Cycle 4 Day 1 (n=5, 2)	-2.8 (± 5.76)	9.5 (± 3.54)		
CFB at Cycle 5 Day 1 (n=130, 143)	0.88 (± 6.87)	1.26 (± 6.1)		
CFB at End of Induction Treatment (n=131, 141)	1.88 (± 7.18)	0.79 (± 7.99)		
CFB at Follow-up Month 2 (n=90, 121)	3.63 (± 6.86)	2.48 (± 6.19)		
CFB at Follow-up Month 4 (n=81, 109)	2.7 (± 7.08)	2.55 (± 6.3)		
CFB at Follow-up Month 6 (n=69, 97)	2.57 (± 6.65)	3.45 (± 6.36)		
CFB at Follow-up Month 8 (n=61, 88)	1.63 (± 6.16)	3.04 (± 6.34)		
CFB at Follow-up Month 10 (n=47, 72)	1.69 (± 7.1)	2.61 (± 6.41)		
CFB at Follow-up Month 12 (n=38, 73)	2.53 (± 7.35)	3.23 (± 6.5)		
CFB at Follow-up Month 14 (n=32, 65)	0.37 (± 7.27)	3.09 (± 6.02)		
CFB at Follow-up Month 16 (n=25, 61)	0 (± 9.58)	3.62 (± 6.5)		
CFB at Follow-up Month 18 (n=23, 51)	1.69 (± 7.33)	3.07 (± 7.37)		
CFB at Follow-up Month 20 (n=21, 42)	1.33 (± 8.47)	3.14 (± 7.4)		
CFB at Follow-up Month 22 (n=16, 38)	1.19 (± 8.24)	3.17 (± 6.94)		
CFB at Follow-up Month 24 (n=15, 33)	0.4 (± 5.91)	3.25 (± 6.97)		
CFB at Final Follow-up (n=58, 61)	1.27 (± 7.04)	1.6 (± 7.73)		
CFB at Extension Follow-up Month 6 (n=7, 17)	1.29 (± 5.5)	4.95 (± 8.23)		
CFB at Extension Follow-up Month 18 (n=1, 1)	-4 (± 99999)	4 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: CFB in Euro Quality of Life 5 Dimension (EuroQoL-5D/EQ-5D) - Health State Profile Utility Score During Induction Phase

End point title	CFB in Euro Quality of Life 5 Dimension (EuroQoL-5D/EQ-5D) - Health State Profile Utility Score During Induction Phase
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End point description:

EQ-5D: participant rated questionnaire which assesses level of current health for 5 domains: mobility, self-care, usual activities, pain and discomfort, anxiety and depression; 1 indicates better health state; 3 indicates worst health state. Score is transformed, results in total score range -0.594 to 1.000; higher score indicates better health state. In timeframe, follow-up months represents months after end of induction (e.g. Follow-up Month 2 is 2 months after end of induction). For 'Obinutuzumab+Bendamustine' arm, participants who had follow-up Months 2 and 4 visits before start of maintenance treatment were reported in induction phase under "CFB at Follow-up Month 2" and "CFB at Follow-up Month 4" categories. ITT population. Here, number of participants analyzed signified those participants who were evaluable for this outcome; "n" signified those participants who were evaluable for specified time point. Number 99999 signified data not available as no participant was evaluable.

End point type	Secondary
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End point timeframe:

Baseline, Day 1 of Cycles 1, 3, 4, 5, End of induction treatment (up to Month 6); Follow-up Months 2, and 4

End point values	Bendamustine Alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	180	185		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=180, 185)	0.77 (± 0.23)	0.79 (± 0.2)		
CFB at Cycle 1 Day 1 (n=0, 0)	99999 (± 99999)	99999 (± 99999)		
CFB at Cycle 3 Day 1 (n=147, 156)	0.03 (± 0.21)	0 (± 0.2)		
CFB at Cycle 4 Day 1 (n=5, 3)	-0.1 (± 0.23)	-0.07 (± 0.41)		
CFB at Cycle 5 Day 1 (n=130, 146)	0.01 (± 0.21)	0.02 (± 0.22)		
CFB at End of Induction Treatment (n=123, 135)	0.03 (± 0.2)	0 (± 0.22)		
CFB at Follow-up Month 2 (n=32, 122)	0.07 (± 0.26)	0.03 (± 0.15)		
CFB at Follow-up Month 4 (n=0, 2)	99999 (± 99999)	-0.12 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: CFB in EuroQol 5D (EQ-5D) - Health State Profile Utility Score During Maintenance Phase

End point title	CFB in EuroQol 5D (EQ-5D) - Health State Profile Utility Score During Maintenance Phase ^[2]
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End point description:

EQ-5D: participant rated questionnaire to assess health-related QoL in terms of single utility score. It assesses level of current health for 5 domains: mobility, self-care, usual activities, pain and discomfort, anxiety and depression; 1 indicates better health state; 3 indicates worst health state. Score is transformed and results in total score range -0.594 to 1.000; higher score indicates better health state. Data for this outcome was planned to be reported only for 'Obinutuzumab + Bendamustine' arm as 'Bendamustine Alone' arm did not have maintenance phase treatment. In timeframe, follow-up months represents months after end of induction (e.g. Follow-up Month 2 is 2 months after end of induction). Follow-up months were during maintenance phase. ITT population (Obinutuzumab + Bendamustine arm only). Here, number of participants analyzed signified those participants who were evaluable for this

outcome; "n" signified those participants who were evaluable for a specified time point.

End point type	Secondary
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End point timeframe:

Baseline, Follow-up Months 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, Final follow-up (up to 2 years after end of induction) (End of induction = up to Month 6)

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint was applicable for only "Obinutuzumab + Bendamustine" arm.

End point values	Obinutuzumab + Bendamustine			
Subject group type	Reporting group			
Number of subjects analysed	143			
Units: units on a scale				
arithmetic mean (standard deviation)				
CFB at Follow-up Month 2 (n=2)	-0.15 (± 0.22)			
CFB at Follow-up Month 4 (n=106)	0.02 (± 0.19)			
CFB at Follow-up Month 6 (n=93)	0.02 (± 0.16)			
CFB at Follow-up Month 8 (n=82)	0.02 (± 0.17)			
CFB at Follow-up Month 10 (n=70)	0.03 (± 0.14)			
CFB at Follow-up Month 12 (n=66)	0.05 (± 0.14)			
CFB at Follow-up Month 14 (n=58)	0.04 (± 0.13)			
CFB at Follow-up Month 16 (n=56)	0.03 (± 0.14)			
CFB at Follow-up Month 18 (n=47)	0.03 (± 0.12)			
CFB at Follow-up Month 20 (n=40)	0.05 (± 0.13)			
CFB at Follow-up Month 22 (n=39)	0.04 (± 0.21)			
CFB at Follow-up Month 24 (n=33)	0.02 (± 0.21)			
CFB at Final Follow-up (n=21)	0.02 (± 0.13)			

Statistical analyses

No statistical analyses for this end point

Secondary: CFB in EQ-5D Visual Analogue Scale (VAS) Score During Induction Phase

End point title	CFB in EQ-5D Visual Analogue Scale (VAS) Score During Induction Phase
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End point description:

EQ-5D: participant rated questionnaire to assess health-related quality of life in terms of a single index value. VAS component rates current health state on a scale from 0 millimeter (mm) (worst imaginable health state) to 100 mm (best imaginable health state); higher scores indicate better health state. In timeframe, follow-up months represents months after end of induction (e.g. Follow-up Month 2 is 2 months after end of induction). For 'Obinutuzumab + Bendamustine' arm, participants who had their follow-up Month 2 and 4 visits before start of maintenance treatment were reported in induction phase results under "CFB at Follow-up Month 2" and "CFB at Follow-up Month 4" categories. ITT population. Here, number of participants analyzed signified those participants who were evaluable for this outcome and "n" signified those participants who were evaluable for a specified time point. The number 99999 signified data not available because no participant was evaluable for this time point.

End point type	Secondary
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End point timeframe:

Baseline, Day 1 of Cycles 1, 3, 4, 5, End of induction treatment (up to Month 6); Follow-up Months 2 and 4

End point values	Bendamustine Alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	178	178		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=178, 178)	-69.39 (± 20.61)	68.03 (± 21.33)		
CFB at Cycle 1 Day 1 (n=0, 0)	99999 (± 99999)	99999 (± 99999)		
CFB at Cycle 3 Day 1 (n=143, 146)	0.5 (± 19.26)	3.48 (± 16.09)		
CFB at Cycle 4 Day 1 (n=5, 3)	-14 (± 33.29)	-4.33 (± 42.15)		
CFB at Cycle 5 Day 1 (n=125, 133)	-0.29 (± 20.89)	5.26 (± 17.66)		
CFB at End of Induction Treatment (n=119, 129)	6.75 (± 64.84)	6.09 (± 22.48)		
CFB at Follow-up Month 2 (n=30, 114)	5.2 (± 20.48)	7.43 (± 18.97)		
CFB at Follow-up Month 4 (n=0, 2)	99999 (± 99999)	0 (± 14.14)		

Statistical analyses

No statistical analyses for this end point

Secondary: CFB in EQ-5D VAS Score During Maintenance Phase

End point title	CFB in EQ-5D VAS Score During Maintenance Phase ^[3]
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End point description:

EQ-5D: participant rated questionnaire to assess health-related quality of life in terms of a single index value. The VAS component rates current health state on a scale from 0 mm (worst imaginable health state) to 100 mm (best imaginable health state); higher scores indicate a better health state. Data for this outcome was planned to be reported only for 'Obinutuzumab + Bendamustine' arm. In timeframe, follow-up months represents months after end of induction (e.g. Follow-up Month 2 is 2 months after end of induction). Follow-up months were during maintenance phase. ITT population (Obinutuzumab + Bendamustine arm only). Here, number of participants analyzed signified those participants who were evaluable for this outcome and "n" signified those participants who were evaluable for a specified time point. The number 99999 signified data not available as only one participant was evaluable for this time point.

End point type	Secondary
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End point timeframe:

Baseline, Follow-up Months 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, Final Follow-up (up to 2 years after end of induction) (end of induction = up to Month 6)

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint was applicable for only "Obinutuzumab + Bendamustine" arm.

End point values	Obinutuzumab + Bendamustine			
Subject group type	Reporting group			
Number of subjects analysed	143			
Units: units on a scale				
arithmetic mean (standard deviation)				
CFB at Follow-up Month 2 (n=1)	-40 (± 99999)			
CFB at Follow-up Month 4 (n=98)	5.96 (± 19.8)			
CFB at Follow-up Month 6 (n=87)	7.21 (± 18.91)			
CFB at Follow-up Month 8 (n=76)	5.62 (± 16.78)			
CFB at Follow-up Month 10 (n=65)	6.08 (± 15.26)			
CFB at Follow-up Month 12 (n=62)	5.82 (± 16.57)			
CFB at Follow-up Month 14 (n=54)	6.76 (± 16.59)			
CFB at Follow-up Month 16 (n=53)	6.91 (± 18.37)			
CFB at Follow-up Month 18 (n=44)	4.5 (± 20.6)			
CFB at Follow-up Month 20 (n=38)	5.76 (± 16.48)			
CFB at Follow-up Month 22 (n=35)	6.14 (± 17.3)			
CFB at Follow-up Month 24 (n=30)	5.67 (± 18.71)			
CFB at Final Follow-up (n=20)	1.05 (± 9.48)			

Statistical analyses

No statistical analyses for this end point

Secondary: CFB in Functional Assessment of Cancer Therapy - Generic (FACT-G) Score

End point title	CFB in Functional Assessment of Cancer Therapy - Generic (FACT-G) Score
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End point description:

The FACT-G is the sum of 4 sub-scales (physical, social, emotional and functional well-being) of FACT-Lym which includes total 27 items; responses to each item range from 0, "Not at all" to 4, "Very much". Total score ranges from 0-108. Higher scores indicate a better PRO/QoL. In timeframe, follow-up months represents months after end of induction (e.g. Follow-up Month 2 is 2 months after end of induction) and extension follow-up months represents months after end of 2 years normal follow-up (e.g. extension follow-up Month 6 is 6 months after end of normal 2 year follow-up). ITT population. Here, number of participants analyzed signified those participants who were evaluable for this outcome and "n" signified those participants who were evaluable for a specified time point. The Number 99999 signified data not available either because no participant or only one participant was evaluable.

End point type	Secondary
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End point timeframe:

Baseline, Day 1 of Cycles 1, 3, 4, 5, End of induction treatment (up to Month 6); Follow-up Months 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, Final Follow-up (up to 2 years after end of induction); Extension follow-up Months 6 and 18

End point values	Bendamustine Alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	177		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=179, 177)	80.07 (± 15.87)	80.61 (± 16.19)		
CFB at Cycle 1 Day 1 (n=0, 0)	99999 (± 99999)	99999 (± 99999)		
CFB at Cycle 3 Day 1 (n=144, 147)	-2.43 (± 12.28)	-0.02 (± 10.49)		
CFB at Cycle 4 Day 1 (n=5, 2)	-9.37 (± 9.89)	0.52 (± 4.98)		
CFB at Cycle 5 Day 1 (n=128, 137)	-3.28 (± 11.72)	-0.04 (± 11.37)		
CFB at End of Induction Treatment (n=129, 133)	-2.23 (± 13.8)	-1.08 (± 11.87)		
CFB at Follow-up Month 2 (n=90, 119)	0.96 (± 13.78)	1.15 (± 12)		
CFB at Follow-up Month 4 (n=80, 107)	2.34 (± 11.13)	2.84 (± 12.92)		
CFB at Follow-up Month 6 (n=65, 93)	2.28 (± 10.1)	3.33 (± 11.52)		
CFB at Follow-up Month 8 (n=61, 86)	-0.54 (± 10.15)	2.14 (± 11.73)		
CFB at Follow-up Month 10 (n=46, 68)	1.17 (± 11.14)	3.44 (± 12.4)		
CFB at Follow-up Month 12 (n=38, 70)	1.63 (± 11.44)	2.98 (± 15.28)		
CFB at Follow-up Month 14 (n=32, 61)	2.77 (± 9.85)	2.44 (± 12.25)		
CFB at Follow-up Month 16 (n=26, 59)	0.8 (± 8.22)	4.37 (± 13.4)		
CFB at Follow-up Month 18 (n=22, 50)	0.65 (± 12.12)	3.99 (± 15.03)		
CFB at Follow-up Month 20 (n=22, 41)	-2.2 (± 12.18)	2.98 (± 16.64)		
CFB at Follow-up Month 22 (n=16, 38)	-3.97 (± 12.71)	0.86 (± 13.96)		
CFB at Follow-up Month 24 (n=15, 33)	-4.43 (± 8.13)	2.57 (± 15.49)		
CFB at Final Follow-up (n=58, 58)	-1.47 (± 11.29)	0.72 (± 17.13)		
CFB at Extension Follow Up Month 6 (n=7, 18)	0.52 (± 11.58)	5.46 (± 15.99)		
CFB at Extension Follow Up Month 18 (n=1, 1)	-1 (± 99999)	25 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: CFB in FACT-Lym Trial Outcome Index (TOI)

End point title	CFB in FACT-Lym Trial Outcome Index (TOI)
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End point description:

TOI is the sum of 3 sub-scales (physical well-being, functional well-being, and Lymphoma sub-scale) of FACT-Lym which includes total 29 items; responses to each item range from 0, "Not at all" to 4, "Very much". Total score ranges from 0–116. Higher scores indicate a better PRO/QoL. In timeframe, follow-up months represents months after end of induction (e.g. Follow-up Month 2 is 2 months after end of induction) and extension follow-up months represents months after end of 2 years normal follow-up (e.g. extension follow-up Month 6 is 6 months after end of normal 2 year follow-up). ITT population. Here, number of participants analyzed signified those participants who were evaluable for this outcome and "n" signified those participants who were evaluable for a specified time point. The Number 99999 signified data not available either because no participant or only one participant was evaluable.

End point type	Secondary
End point timeframe:	
Baseline, Day 1 of Cycles 1, 3, 4, 5, End of induction treatment (up to Month 6); Follow-up Months 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, Final Follow-up (up to 2 years after end of induction); Extension follow-up Months 6 and 18	

End point values	Bendamustine Alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	184	186		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=184, 186)	84.79 (± 19.01)	84.53 (± 19.03)		
CFB at Cycle 1 Day 1 (n=0, 0)	99999 (± 99999)	99999 (± 99999)		
CFB at Cycle 3 Day 1 (n=149, 158)	-2.61 (± 18.09)	1.6 (± 14.03)		
CFB at Cycle 4 Day 1 (n=5, 3)	-10.4 (± 10.38)	26.44 (± 19.51)		
CFB at Cycle 5 Day 1 (n=132, 146)	-1.55 (± 15.6)	2.23 (± 14.34)		
CFB at End of Induction Treatment (n=134, 142)	-0.4 (± 17.9)	0.44 (± 16.73)		
CFB at Follow-up Month 2 (n=91, 125)	3.63 (± 15.93)	4.81 (± 14.98)		
CFB at Follow-up Month 4 (n=81, 113)	3.75 (± 13.67)	5.16 (± 17.03)		
CFB at Follow-up Month 6 (n=69, 97)	3.34 (± 12.36)	6.56 (± 13.08)		
CFB at Follow-up Month 8 (n=62, 89)	0.68 (± 12.96)	6.25 (± 14.09)		
CFB at Follow-up Month 10 (n=47, 74)	2.42 (± 13.99)	5.3 (± 16.66)		
CFB at Follow-up Month 12 (n=38, 73)	4.14 (± 14.46)	6.92 (± 16.37)		
CFB at Follow-up Month 14 (n=32, 65)	1.98 (± 12.49)	5.82 (± 14.5)		
CFB at Follow-up Month 16 (n=26, 62)	-1.46 (± 15.97)	6.93 (± 16.65)		
CFB at Follow-up Month 18 (n=23, 52)	0.69 (± 12.84)	7.57 (± 16.55)		
CFB at Follow-up Month 20 (n=22, 44)	-2.03 (± 16.54)	7.01 (± 18.23)		
CFB at Follow-up Month 22 (n=16, 41)	-1.28 (± 11.66)	3.29 (± 23.02)		
CFB at Follow-up Month 24 (n=15, 35)	-2.69 (± 10.7)	6.75 (± 21.25)		
CFB at Final Follow-up (n=59, 63)	-0.9 (± 15.31)	4.8 (± 18.47)		
CFB at Extension Follow Up Month 6 (n=7, 18)	3.05 (± 11.34)	5.6 (± 20.67)		
CFB at Extension Follow Up Month 18 (n=1, 1)	-5 (± 99999)	11 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: CFB in FACT-Lym Total Score

End point title	CFB in FACT-Lym Total Score
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End point description:

FACT-Lym total score: sum of physical well-being score (7 items), social/family well-being (7 items), emotional well-being (6 items), functional well-being (7 items), and Lymphoma sub-scale (15 items); responses to each item range from 0, "Not at all" to 4, "Very much". Total score ranges from 0–168. Higher scores indicate better PRO/QoL. In timeframe, follow-up months represents months after end of induction (e.g. Follow-up Month 2 is 2 months after end of induction) and extension follow-up months represents months after end of 2 years normal follow-up (e.g. extension follow-up Month 6 is 6 months after end of normal 2 year follow-up). ITT population. Here, number of participants analyzed signified those participants who were evaluable for this outcome and "n" signified those participants who were evaluable for a specified time point. Number 99999 signified data not available either because no participant or only one participant was evaluable.

End point type	Secondary
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End point timeframe:

Baseline, Day 1 of Cycles 1, 3, 4, 5, End of induction treatment (up to Month 6); Follow-up Months 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, Final Follow-up (up to 2 years after end of induction); Extension follow-up Months 6 and 18

End point values	Bendamustine Alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	180	177		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=180, 177)	124.86 (± 23.63)	126 (± 23.96)		
CFB at Cycle 1 Day 1 (n=0, 0)	99999 (± 99999)	99999 (± 99999)		
CFB at Cycle 3 Day 1 (n=143, 147)	-1.61 (± 17.85)	1 (± 13.96)		
CFB at Cycle 4 Day 1 (n=5, 2)	-12.16 (± 14.8)	22.53 (± 16.23)		
CFB at Cycle 5 Day 1 (n=128, 136)	-2.37 (± 16.63)	1.47 (± 15.44)		
CFB at End of Induction Treatment (n=130, 133)	-0.11 (± 18.91)	0.25 (± 18.5)		
CFB at Follow-up Month 2 (89, 117)	4.74 (± 18.22)	3.48 (± 15.18)		
CFB at Follow-up Month 4 (n=80, 105)	5.14 (± 16.39)	5.57 (± 17.28)		
CFB at Follow-up Month 6 (n=66, 95)	5.08 (± 14.88)	6.85 (± 15.59)		
CFB at Follow-up Month 8 (n=61, 86)	1.23 (± 14.48)	5.46 (± 15.84)		
CFB at Follow-up Month 10 (n=47, 70)	3.2 (± 16.87)	5.74 (± 17.58)		
CFB at Follow-up Month 12 (n= 38, 71)	4.19 (± 17.76)	6.41 (± 20.02)		
CFB at Follow-up Month 14 (n= 32, 62)	3.13 (± 14.51)	5.97 (± 17.35)		
CFB at Follow-up Month 16 (n=25, 59)	1.18 (± 14.22)	8.49 (± 17.45)		
CFB at Follow-up Month 18 (n=22, 49)	2.11 (± 16.99)	7.33 (± 20.14)		
CFB at Follow-up Month 20 (n=21, 40)	-0.92 (± 16.7)	6.16 (± 21.85)		
CFB at Follow-up Month 22 (n=16, 37)	-2.66 (± 14.13)	4.74 (± 20.21)		
CFB at Follow-up Month 24 (n=15, 32)	-3.98 (± 11.86)	6.11 (± 21.48)		
CFB at Final follow-up (n=58, 56)	-0.18 (± 16.66)	2.86 (± 22.89)		
CFB at Extension Follow Up Month 6 (n=7, 17)	1.8 (± 16.55)	10.93 (± 22.57)		
CFB at Extension Follow Up Month 18 (n=1, 1)	-5 (± 99999)	29 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Deterioration of FACT-Lym TOI

End point title	Time to Deterioration of FACT-Lym TOI
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End point description:

The median time, in month, from date of randomization until a clinically meaningful decline from baseline in TOI or death, whichever occurred first. TOI: sum of physical well-being score, functional well-being score, and Lymphoma sub-scale of FACT-Lym; total 29 items, responses to each item range from 0, "Not at all" to 4, "Very much". Total score ranges from 0-116. Higher scores indicate a better PRO/QoL. A clinically meaningful decline in TOI score was defined as at least a 6 point decline from baseline. Time to deterioration was estimated using Kaplan-Meier method and 95% CI for median was computed using the method of Brookmeyer and Crowley. In timeframe, follow-up months represents months after end of induction (EOI) (e.g. Follow-up Month 2 is 2 months after EOI) and extension follow-up months represents months after end of 2 years normal follow-up (e.g. extension follow-up Month 6 is 6 months after end of normal 2 year follow-up). ITT population.

End point type	Secondary
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End point timeframe:

Baseline up to approximately 4 years (Baseline, Day 1 of Cycles 1, 3, 4, 5, EOI treatment [up to Month 6]; Follow-up Months 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, Final Follow-up [up to 2 years after EOI]; Extension follow-up Months 6 and 18)

End point values	Bendamustine Alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	194		
Units: months				
median (confidence interval 95%)	4.6 (3.8 to 6.4)	8 (5.8 to 15.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Definitive Improvement (DI) From Baseline in FACT-Lym Instrument Scores

End point title	Percentage of Participants With Definitive Improvement (DI) From Baseline in FACT-Lym Instrument Scores
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End point description:

FACT-Lym: 42-items in 5 subscales. Responses to each item range from 0 (Not at all) to 4 (Very much). FACT-Lym Lymphoma subscale includes 15 items (total score range = 0-60). FACT-Lym TOI is sum of 3 subscales (physical well-being, functional well-being, lymphoma subscale) and includes 29 items (total score range = 0-116). FACT-Lym total score is sum of 42 items (total score ranges from 0-168). For all above, higher scores indicate a better PRO/QoL. DI from baseline: at least 3 point increase from

baseline in FACT-Lym Lymphoma subscale; at least 6 point increase from baseline in FACT Lym TOI; at least 7 point increase from baseline in FACT Lym total scores. In timeframe, follow-up months represents months after EOI (e.g. Follow-up Month 2 is 2 months after EOI; EOI = up to Month 6). ITT population. Here, number of participants analyzed signified those participants who were evaluable for this outcome and "n" signified those participants who were evaluable for a specified category.

End point type	Secondary
End point timeframe:	
Baseline, Cycle 5 Day 1 (C5D1) (Cycle length = 28 days), Follow-up Months 6 (FUM6), and 12 (FUM12)	

End point values	Bendamustine Alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	184	186		
Units: percentage of participants				
number (not applicable)				
DI in Lymphoma sub-scale: C5D1 (n=142, 148)	31	41.2		
DI in Lymphoma sub-scale: FUM6 (n=76, 99)	38.2	48.5		
DI in Lymphoma sub-scale: FUM12 (n=44, 77)	38.6	48.1		
DI in FACT Lym TOI: C5D1 (n=143, 149)	22.4	34.9		
DI in FACT Lym TOI: FUM6 (n=77, 99)	28.6	43.4		
DI in FACT Lym TOI: FUM12 (n=44, 77)	27.3	48.1		
DI in FACT Total: C5D1 (n=143, 149)	23.1	27.5		
DI in FACT Total: FUM6 (n=77, 99)	33.8	42.4		
DI in FACT Total: FUM12 (n=44, 77)	29.5	45.5		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 4.5 years

Adverse event reporting additional description:

Safety population included all participants who received any amount of obinutuzumab or bendamustine therapy.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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Reporting groups

Reporting group title	Obinutuzumab + Bendamustine
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Reporting group description:

Induction phase: Participants received Bendamustine 90 mg/m² IV on Days 2 and 3 of Cycle 1 and on Days 1 and 2 of Cycles 2-6 (28-day cycles) for the first 10 participants and on Days 1 and 2 of each 28-day cycle for Cycles 1-6 for remaining participants. Participants also received obinutuzumab 1000 mg IV infusion on Days 1, 8, and 15 of Cycle 1; Day 1 of Cycles 2-6.

Maintenance phase: Participants received obinutuzumab 1000 mg IV infusion every 2 months until disease progression or for up to 2 years (whichever occurred first).

Reporting group title	Bendamustine Alone
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Reporting group description:

Participants received Bendamustine 120 mg/m² IV infusion on Days 1 and 2 of each 28-day cycle for up to six cycles.

Serious adverse events	Obinutuzumab + Bendamustine	Bendamustine Alone	
Total subjects affected by serious adverse events			
subjects affected / exposed	74 / 194 (38.14%)	65 / 198 (32.83%)	
number of deaths (all causes)	42	56	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 194 (0.52%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	1 / 1	1 / 1	
Adenocarcinoma			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bladder cancer			

subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangiocarcinoma			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal cancer			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Leiomyosarcoma			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukaemia			
subjects affected / exposed	0 / 194 (0.00%)	2 / 198 (1.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Malignant melanoma			
subjects affected / exposed	1 / 194 (0.52%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	2 / 194 (1.03%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraneoplastic pemphigus			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polycythaemia vera			

subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
T-cell lymphoma			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Thyroid neoplasm			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	2 / 194 (1.03%)	2 / 198 (1.01%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 194 (0.00%)	2 / 198 (1.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

General physical health deterioration			
subjects affected / exposed	2 / 194 (1.03%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthermia			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza like illness			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	5 / 194 (2.58%)	3 / 198 (1.52%)	
occurrences causally related to treatment / all	2 / 5	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Graft versus host disease			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Social circumstances			
Social problem			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social stay hospitalisation			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chylothorax			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emphysema			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			

subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 194 (0.52%)	3 / 198 (1.52%)	
occurrences causally related to treatment / all	1 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mania			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	2 / 194 (1.03%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infusion related reaction			
subjects affected / exposed	6 / 194 (3.09%)	3 / 198 (1.52%)	
occurrences causally related to treatment / all	6 / 6	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaw fracture			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural bile leak			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seroma			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stab wound			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pseudoaneurysm			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Wrist fracture			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 194 (1.03%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			

subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	2 / 194 (1.03%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 194 (0.52%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paroxysmal arrhythmia			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Central nervous system lesion			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 194 (0.52%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Presyncope			

subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	2 / 194 (1.03%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Anaemia			
subjects affected / exposed	3 / 194 (1.55%)	3 / 198 (1.52%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	8 / 194 (4.12%)	6 / 198 (3.03%)	
occurrences causally related to treatment / all	12 / 13	6 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	6 / 194 (3.09%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	5 / 6	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			

subjects affected / exposed	4 / 194 (2.06%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Necrotising retinitis			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fissure			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	2 / 194 (1.03%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 194 (0.00%)	4 / 198 (2.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			

subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	2 / 194 (1.03%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 194 (1.03%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			

subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pollakiuria			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure chronic			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ureteric obstruction			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary incontinence			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Muscle haemorrhage			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Osteoarthritis			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Atypical pneumonia			
subjects affected / exposed	1 / 194 (0.52%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 194 (0.00%)	2 / 198 (1.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	2 / 194 (1.03%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Fungal sepsis			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastroenteritis			

subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastroenteritis norovirus			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis B			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	2 / 194 (1.03%)	3 / 198 (1.52%)	
occurrences causally related to treatment / all	2 / 2	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 194 (0.00%)	2 / 198 (1.01%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	3 / 194 (1.55%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	1 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	1 / 194 (0.52%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumocystis jirovecii pneumonia			

subjects affected / exposed	1 / 194 (0.52%)	2 / 198 (1.01%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	2 / 2	
Pneumonia			
subjects affected / exposed	5 / 194 (2.58%)	10 / 198 (5.05%)	
occurrences causally related to treatment / all	2 / 5	6 / 10	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia cytomegaloviral			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonal sepsis			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Sepsis			
subjects affected / exposed	6 / 194 (3.09%)	7 / 198 (3.54%)	
occurrences causally related to treatment / all	3 / 6	4 / 7	
deaths causally related to treatment / all	0 / 1	1 / 3	
Sinusitis			
subjects affected / exposed	2 / 194 (1.03%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth infection			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			

subjects affected / exposed	2 / 194 (1.03%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	3 / 194 (1.55%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 194 (0.52%)	2 / 198 (1.01%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	1 / 194 (0.52%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 194 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour lysis syndrome			
subjects affected / exposed	0 / 194 (0.00%)	2 / 198 (1.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Obinutuzumab + Bendamustine	Bendamustine Alone	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	187 / 194 (96.39%)	187 / 198 (94.44%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	22 / 194 (11.34%)	1 / 198 (0.51%)	
occurrences (all)	25	2	
Phlebitis			
subjects affected / exposed	11 / 194 (5.67%)	13 / 198 (6.57%)	
occurrences (all)	11	14	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	29 / 194 (14.95%)	23 / 198 (11.62%)	
occurrences (all)	40	32	
Chest pain			
subjects affected / exposed	10 / 194 (5.15%)	3 / 198 (1.52%)	
occurrences (all)	10	3	
Chills			
subjects affected / exposed	24 / 194 (12.37%)	20 / 198 (10.10%)	
occurrences (all)	26	23	
Fatigue			
subjects affected / exposed	76 / 194 (39.18%)	66 / 198 (33.33%)	
occurrences (all)	144	113	
Oedema peripheral			
subjects affected / exposed	12 / 194 (6.19%)	14 / 198 (7.07%)	
occurrences (all)	13	17	
Pain			
subjects affected / exposed	5 / 194 (2.58%)	10 / 198 (5.05%)	
occurrences (all)	6	10	
Pyrexia			
subjects affected / exposed	50 / 194 (25.77%)	33 / 198 (16.67%)	
occurrences (all)	74	40	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	54 / 194 (27.84%)	34 / 198 (17.17%)	
occurrences (all)	72	39	

Dyspnoea			
subjects affected / exposed	22 / 194 (11.34%)	21 / 198 (10.61%)	
occurrences (all)	23	26	
Nasal congestion			
subjects affected / exposed	16 / 194 (8.25%)	5 / 198 (2.53%)	
occurrences (all)	17	6	
Oropharyngeal pain			
subjects affected / exposed	11 / 194 (5.67%)	7 / 198 (3.54%)	
occurrences (all)	14	7	
Rhinorrhoea			
subjects affected / exposed	11 / 194 (5.67%)	3 / 198 (1.52%)	
occurrences (all)	11	3	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	21 / 194 (10.82%)	21 / 198 (10.61%)	
occurrences (all)	24	26	
Investigations			
Weight decreased			
subjects affected / exposed	9 / 194 (4.64%)	17 / 198 (8.59%)	
occurrences (all)	9	17	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	123 / 194 (63.40%)	113 / 198 (57.07%)	
occurrences (all)	281	238	
Nervous system disorders			
Dizziness			
subjects affected / exposed	13 / 194 (6.70%)	17 / 198 (8.59%)	
occurrences (all)	20	23	
Dysgeusia			
subjects affected / exposed	15 / 194 (7.73%)	16 / 198 (8.08%)	
occurrences (all)	20	20	
Headache			
subjects affected / exposed	26 / 194 (13.40%)	32 / 198 (16.16%)	
occurrences (all)	35	37	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	23 / 194 (11.86%)	28 / 198 (14.14%)	
occurrences (all)	36	34	
Neutropenia			
subjects affected / exposed	66 / 194 (34.02%)	56 / 198 (28.28%)	
occurrences (all)	126	92	
Thrombocytopenia			
subjects affected / exposed	26 / 194 (13.40%)	47 / 198 (23.74%)	
occurrences (all)	54	87	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	7 / 194 (3.61%)	11 / 198 (5.56%)	
occurrences (all)	7	12	
Abdominal pain			
subjects affected / exposed	12 / 194 (6.19%)	18 / 198 (9.09%)	
occurrences (all)	13	21	
Abdominal pain upper			
subjects affected / exposed	10 / 194 (5.15%)	15 / 198 (7.58%)	
occurrences (all)	11	19	
Constipation			
subjects affected / exposed	41 / 194 (21.13%)	38 / 198 (19.19%)	
occurrences (all)	54	53	
Diarrhoea			
subjects affected / exposed	53 / 194 (27.32%)	59 / 198 (29.80%)	
occurrences (all)	71	78	
Dry mouth			
subjects affected / exposed	8 / 194 (4.12%)	11 / 198 (5.56%)	
occurrences (all)	8	14	
Dyspepsia			
subjects affected / exposed	12 / 194 (6.19%)	8 / 198 (4.04%)	
occurrences (all)	15	10	
Nausea			
subjects affected / exposed	104 / 194 (53.61%)	121 / 198 (61.11%)	
occurrences (all)	204	220	
Vomiting			

subjects affected / exposed occurrences (all)	42 / 194 (21.65%) 63	54 / 198 (27.27%) 87	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	10 / 194 (5.15%)	4 / 198 (2.02%)	
occurrences (all)	11	4	
Pruritus			
subjects affected / exposed	25 / 194 (12.89%)	12 / 198 (6.06%)	
occurrences (all)	33	13	
Rash			
subjects affected / exposed	24 / 194 (12.37%)	23 / 198 (11.62%)	
occurrences (all)	30	26	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	23 / 194 (11.86%)	9 / 198 (4.55%)	
occurrences (all)	28	10	
Back pain			
subjects affected / exposed	13 / 194 (6.70%)	18 / 198 (9.09%)	
occurrences (all)	14	22	
Myalgia			
subjects affected / exposed	12 / 194 (6.19%)	15 / 198 (7.58%)	
occurrences (all)	13	17	
Pain in extremity			
subjects affected / exposed	18 / 194 (9.28%)	10 / 198 (5.05%)	
occurrences (all)	22	13	
Infections and infestations			
Bronchitis			
subjects affected / exposed	18 / 194 (9.28%)	17 / 198 (8.59%)	
occurrences (all)	29	21	
Herpes zoster			
subjects affected / exposed	6 / 194 (3.09%)	13 / 198 (6.57%)	
occurrences (all)	6	15	
Nasopharyngitis			
subjects affected / exposed	17 / 194 (8.76%)	8 / 198 (4.04%)	
occurrences (all)	22	10	
Sinusitis			

subjects affected / exposed occurrences (all)	22 / 194 (11.34%) 32	10 / 198 (5.05%) 12	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	23 / 194 (11.86%) 28	15 / 198 (7.58%) 18	
Urinary tract infection subjects affected / exposed occurrences (all)	18 / 194 (9.28%) 29	11 / 198 (5.56%) 13	
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	34 / 194 (17.53%) 36	35 / 198 (17.68%) 47	
Hypokalaemia subjects affected / exposed occurrences (all)	14 / 194 (7.22%) 20	12 / 198 (6.06%) 15	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 December 2009	The protocol was amended to address feedback from the FDA during the Type B (pre Phase III) meeting held on 03 November 2009. The protocol was amended to modify bendamustine control arm dosing regimen from 90 mg/m ² to 120 mg/m ² which was given on Days 1 and 2 of a 28-day cycle, definition of rituximab-refractoriness was more clearly defined in the inclusion criteria. Eligibility criteria was also modified in order to allow more sites and countries to participate in the study.
28 July 2010	The protocol was amended to address feedback from the investigators and others since the first version of the protocol was issued. The exclusion criteria was modified to exclude participants who had received bendamustine; definition of rituximab-refractory iNHL was clarified; exclusion criterion regarding contraception was expanded to include participants who received only bendamustine; an early interim analysis for futility was added to the protocol in response to a recommendation by the independent data monitoring committee (IDMC); analysis of the FACT-Lym questionnaire was modified to capture changes in the participant's health-related QoL based on minimally important differences.
07 December 2011	The protocol was amended to address general issues related to the conduct of the trial, as well as comments from the IDMC, Investigators and study management team. A number of changes were made to eligibility criteria and some parameters were clarified.
01 May 2012	The protocol was amended to address general issues related to the conduct of the trial. The eligibility criteria was modified to allow for the enrollment of participant's previously treated with a bendamustine-containing regimen to reflect clinical practice so that participant's who were previously bendamustine responders and failed a subsequent regimen containing either an alkylating agent or anthracycline were allowed to participate in the study.
27 November 2012	This was a country-specific amendment for France to exclude participant's with a history of progressive multifocal encephalopathy (PML). The section on risks associated with obinutuzumab therapy was also updated with information on PML diagnosis, evaluation and guidance on how to manage a potential PML case.
06 March 2013	The protocol was amended to include revised information about PML; changes were made to some of the efficacy text (PFS assessment, secondary outcome measures and pharmacodynamic assessment) to align the protocol efficacy sections with the statistical analysis plan; requirement of administration of obinutuzumab after bendamustine on days when both drugs are given was deleted, so that the order in which the drugs are given is left to the discretion of the sites.
24 October 2013	The protocol was amended to allow for an increase in the number of participants enrolled from 360 to 410 and to extend the period of AE reporting in the comparator arm; collection of safety data was made consistent over the same timeframe for both treatment arms to more accurately assess the overall benefit/risk profile of adding obinutuzumab to bendamustine; period of AEs reporting in the comparator arm was extended in response to a recommendation by the IDMC; appendix E was also modified to match the original wording of the revised response criteria for malignant lymphoma and current clinical practice.
10 March 2014	The protocol was amended following the identification of a higher incidence of thrombocytopenia and hemorrhagic events in participants with chronic lymphocytic leukemia receiving obinutuzumab; guidelines on the management of participant's with thrombocytopenia (especially during the first cycle), and participants receiving anticoagulants or platelet inhibitors were also added.

07 May 2015	This protocol version is a country-specific amendment implemented in Canada and the Czech Republic. The protocol was amended to offer the choice to participant's in the control arm receiving bendamustine to cross-over to the combination treatment arm (obinutuzumab plus bendamustine).
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported