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	30 November 2018

Results information

Result version number	v2 (current)
This version publication date	18 December 2019
First version publication date	12 October 2016
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	GO01297

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	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, 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	Final
Date of interim/final analysis	30 November 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 November 2018
Was the trial ended prematurely?	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:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 April 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
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: 98
Country: Number of subjects enrolled	Switzerland: 2
Country: Number of subjects enrolled	Czech Republic: 34
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	France: 81
Country: Number of subjects enrolled	United Kingdom: 30
Country: Number of subjects enrolled	Italy: 17
Country: Number of subjects enrolled	Netherlands: 18
Country: Number of subjects enrolled	Russian Federation: 24
Country: Number of subjects enrolled	Sweden: 14
Country: Number of subjects enrolled	United States: 69
Worldwide total number of subjects	413
EEA total number of subjects	220

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)	228
From 65 to 84 years	181
85 years and over	4

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Overall, the ITT population in this final analysis comprised of 413 patients with iNHL (209 patients in the benda arm and 204 patients in the G-benda arm).

Period 1

Period 1 title	Overall Study (overall period)
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 mg/m^2 IV infusion on Days 1 and 2 of each 28-day cycle for up to six cycles.

Arm type	Active comparator
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/m^2 IV infusion on Days 1 and 2 of each 28-day cycle for up to six cycles.

Arm title	Obinutuzumab + Bendamustine

Arm 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 CR, PR or 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/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.

Number of subjects in period 1	Bendamustine alone	Obinutuzumab + Bendamustine
Started	209	204
Completed	0	0
Not completed	209	204
Physician decision	2	4
Consent withdrawn by subject	21	14
Study terminated by Sponsor	82	101
Death	100	84
Lost to follow-up	4	1

Baseline characteristics

Reporting groups	
Reporting group title	Bendamustine alone
Reporting group description:	
Participants received Bendamustine 120 mg/m^2 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 CR, PR or 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	209	204	413
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	113	115	228
From 65-84 years	94	87	181
85 years and over	2	2	4
Age Continuous Units: Years			
arithmetic mean	61.9	62.0	
standard deviation	± 11.5	± 11.3	-
Sex: Female, Male Units: Subjects			
Female	87	88	175
Male	122	116	238
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	5	6	11
Not Hispanic or Latino	174	183	357
Not Stated	30	15	45
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	2	1	3
Asian	3	6	9
Black or African American	3	5	8
Multiple	1	0	1
Unknown	19	12	31

White	181	180	361

End points

End points reporting groups

Reporting group title	Bendamustine alone
Reporting group description:	
Participants received Bendamustine 120 mg/m^2 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 CR, PR or 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.	
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 analyses were done for this endpoint.	

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	204		
Units: participants	125	87		

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

End point description:

PFS was defined as time from randomization to first occurrence of PD or death as assessed by an IRC according to modified response criteria for iNHL (Modified Cheson et al, 2007). PD was defined as 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 (e.g., splenic or hepatic nodules). To be PD, a lymph node with a diameter of short axis of <1.0 cm must increase by ≥ 50% and to a size of 1.5 multiplied by 1.5 cm or more than 1.5 cm in long axis; at least a 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. 9999 = non-estimable number due to higher (>50%) number of censored participants.

End point type	Primary

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	209	204		
Units: months				
median (confidence interval 95%)	14.1 (11.7 to 16.6)	29.2 (20.5 to 9999)		

Statistical analyses

Statistical analysis title	PFS as assessed by IRC analysis
Comparison groups	Bendamustine alone v Obinutuzumab + Bendamustine
Number of subjects included in analysis	413
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	0.7

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

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 ≥ 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.

End point type	Secondary

End point timeframe:

Baseline until PD or death, whichever occurred first (up to 8.5 years overall))

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	204		
Units: participants	152	132		

Statistical analyses

No statistical analyses for this end point

Secondary: PFS as Assessed by Investigator

End point title	PFS as Assessed by Investigator

End point description:

PFS was defined as the time from randomization to the first occurrence of PD as assessed by an investigator according to the modified response criteria for iNHL (Modified Cheson et al, 2007), or death from any cause on study. 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 ≥ 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. PFS was estimated using Kaplan-Meier method and 95% CI for median was computed using the method of Brookmeyer and Crowley.

End point type	Secondary

End point timeframe:

Baseline until PD or death, whichever occurred first (up to 8.5 years overall)

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	204		
Units: months				
median (confidence interval 95%)	14.1 (12.6 to 16.2)	25.8 (20.1 to 36.5)		

Statistical analyses

Statistical analysis title	PFS as assessed by Investigator analysis
Comparison groups	Bendamustine alone v Obinutuzumab + Bendamustine
Number of subjects included in analysis	413
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	0.45
upper limit	0.73

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

End point title	Percentage of Participants With Objective Response as Assessed by IRC

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. IRC review was performed up clinical cutoff date of to 1 May 2015.

End point type	Secondary

End point timeframe:

Baseline until PD or death, whichever occurred first (up to approximately 5 years)

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	204		
Units: percentage of participants				
number (confidence interval 95%)	77.5 (71.24 to 82.98)	75.5 (69.00 to 81.23)		

Statistical analyses

Statistical analysis title	Percentage of Participants With OR
Statistical analysis description:	
Statistical analysis for IRC assessment.	
Comparison groups	Bendamustine alone v Obinutuzumab + Bendamustine
Number of subjects included in analysis	413
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9298
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in response rate
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	1.65

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

End point title	Percentage of Participants With Objective Response as Assessed by Investigator

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.

End point type	Secondary

End point timeframe:

Baseline until PD or death, whichever occurred first (up to approximately 8.5 years)

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	204		
Units: percentage of participants				
number (confidence interval 95%)	83.3 (77.49 to 88.05)	82.4 (76.42 to 87.32)		

Statistical analyses

Statistical analysis title	Percentage of Participants With OR
Statistical analysis description:	
Statistical analysis for investigator assessment.	
Comparison groups	Bendamustine alone v Obinutuzumab + Bendamustine
Number of subjects included in analysis	413
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7857
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in response rate
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.44
upper limit	6.64

Secondary: Percentage of Participants with Best Overall Response (BOR) as Assessed by IRC

End point title	Percentage of Participants with Best Overall Response (BOR) as Assessed by IRC

End point description:

BOR 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 & disease-related symptoms if present prior to therapy, PR: at least 50% regression of measurable disease compared to tumors measured by baseline scan & 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 measurable disease should be present, SD: Failing to attain criteria needed for a CR/PR, but not fulfilling those for PD, 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 single involved node, or size of other lesions (e.g., splenic or hepatic nodules). IRC review was performed up clinical cutoff date of to 1 May 2015.

End point type	Secondary

End point timeframe:

Baseline until PD or death, whichever occurred first (up to approximately 5 years)

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	204		
Units: percentage of participants				
number (confidence interval 95%)				
IRC Assessment: CR	17.2 (12.37 to 23.04)	16.2 (11.40 to 21.96)		
IRC Assessment: PR	60.3 (53.31 to 66.97)	59.3 (52.23 to 66.12)		
IRC Assessment: SD	12.0 (7.89 to 17.15)	13.7 (9.32 to 19.22)		
IRC Assessment: PD	5.7 (3.00 to 9.81)	4.9 (2.38 to 8.83)		
IRC Assessment: Unable to evaluate	1.0 (0.12 to 3.41)	1.0 (0.12 to 3.50)		
IRC Assessment: Missing	3.8 (1.67 to 7.40)	4.9 (2.38 to 8.83)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Best Overall Response (BOR) as Assessed by Investigator

End point title	Percentage of Participants with Best Overall Response (BOR) as Assessed by Investigator

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 other nodes, liver, or spleen; with exception of splenic and hepatic nodules, involvement of other organs is usually assessable and no measurable disease should be present, 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 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 single involved node, or the size of other lesions (e.g., splenic or hepatic nodules).

End point type	Secondary

End point timeframe:

Baseline until PD or death, whichever occurred first (up to approximately 8.5 years)

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	204		
Units: percentage of participants				
number (confidence interval 95%)				
Investigator Assessment: CR	21.5 (16.16 to 27.73)	23.5 (17.89 to 29.96)		

Investigator Assessment: PR	61.7 (54.76 to 68.34)	58.8 (51.74 to 65.65)		
Investigator Assessment: SD	6.7 (3.71 to 10.98)	6.4 (3.44 to 10.65)		
Investigator Assessment: PD	4.8 (2.32 to 8.62)	6.4 (3.44 to 10.65)		
Investigator Assessment: Unable to evaluate	1.4 (0.30 to 4.14)	0.5 (0.01 to 2.70)		
Investigator Assessment: Missing	3.8 (1.67 to 7.40)	4.4 (2.04 to 8.21)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with BOR at the End of induction Treatment as Assessed by IRC

End point title	Percentage of Participants with BOR at the End of induction Treatment as Assessed by IRC

End point description:

BOR 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 & disease-related symptoms if present prior to therapy, PR: at least 50% regression of measurable disease compared to tumors measured by a baseline scan & 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 measurable disease should be present, SD: Failing to attain criteria needed for a CR/PR, but not fulfilling those for PD, 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 the SPD of any previously involved nodes, or in a single involved node, or size of other lesions (e.g., splenic/hepatic nodules). IRC review was performed up clinical cutoff date of to 1 May 2015.

End point type	Secondary

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	209	204		
Units: percentage of participants				
number (confidence interval 95%)				
IRC Assessment: CR	12.0 (7.93 to 17.23)	11.8 (7.69 to 17.00)		
IRC Assessment: PR	52.4 (45.38 to 59.35)	54.9 (47.80 to 61.86)		
IRC Assessment: SD	10.1 (6.36 to 15.02)	11.8 (7.69 to 17.00)		
IRC Assessment: PD	10.6 (6.75 to 15.58)	8.8 (5.31 to 13.59)		
IRC Assessment: Unable to Evaluate	2.9 (1.07 to 6.17)	2.0 (0.54 to 4.94)		
IRC Assessment: Missing	12.0 (7.93 to 17.23)	10.8 (6.88 to 15.87)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with BOR at the End of induction Treatment as Assessed by Investigator

End point title	Percentage of Participants with BOR at the End of induction Treatment as Assessed by Investigator

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 a baseline scan and no new sites; no increase in size of other nodes, liver, or spleen; with exception of splenic and hepatic nodules, involvement of other organs is usually assessable and no measurable disease should be present, SD: Failing to attain 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 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).

End point type	Secondary

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	209	204		
Units: percentage of participants				
number (confidence interval 95%)				
Investigator Assessment: CR	15.8 (11.12 to 21.45)	17.2 (12.25 to 23.04)		
Investigator Assessment: PR	53.1 (46.10 to 60.03)	60.3 (53.23 to 67.06)		
Investigator Assessment: SD	4.3 (1.99 to 8.02)	3.9 (1.71 to 7.58)		
Investigator Assessment: PD	12.0 (7.89 to 17.15)	9.3 (5.70 to 14.16)		
Investigator Assessment: Unable to Evaluate	2.9 (1.06 to 6.14)	0.5 (0.01 to 2.70)		
Investigator Assessment: Missing	12.0 (7.89 to 17.15)	8.8 (5.31 to 13.59)		

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

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

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. IRC review was performed up clinical cutoff date of to 1 May 2015.

End point type	Secondary

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	209	204		
Units: percentage of participants				
number (confidence interval 95%)	64.4 (57.51 to 70.92)	66.7 (59.75 to 73.10)		

Statistical analyses

Statistical analysis title	OR at the End of Induction Treatment
Statistical analysis description:	
Statistical analysis for IRC assessment.	
Comparison groups	Bendamustine alone v Obinutuzumab + Bendamustine
Number of subjects included in analysis	413
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8347
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in response rate
Point estimate	2.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.2
upper limit	11.69

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

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

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.

End point type	Secondary

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	209	204		
Units: percentage of participants				
number (confidence interval 95%)	68.9 (62.15 to 75.11)	77.5 (71.09 to 82.99)		

Statistical analyses

Statistical analysis title	OR at End of Induction Treatment

Statistical analysis description:

Statistical analysis for investigator assessment.

Comparison groups	Bendamustine alone v Obinutuzumab + Bendamustine
Number of subjects included in analysis	413
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0466
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in response rate
Point estimate	8.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.22
upper limit	17.32

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 evidence of disease & disease-related symptoms if present before therapy. PR: at least 50% measurable disease regressed vs. to baseline scan and no new sites; no increase in size of other nodes/liver/spleen; other organs involved is usually assessable; no measurable disease present. PD: any new lesion >1.5 cm in any axis appear 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 estimated using Kaplan-Meier method. IRC review performed up to clinical cutoff date 1 May 2015. 9999 = non-estimable number due to higher (>50%) number of censored participants.

End point type	Secondary

End point timeframe:

Baseline until PD or death, whichever occurred first (up to approximately 5 years)

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	158		
Units: months				
median (confidence interval 95%)	12.7 (10.4 to 14.1)	38.5 (25.4 to 9999)		

Statistical analyses

Statistical analysis title	Duration of Response

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	323
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.31
upper limit	0.61

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

End point title	Duration of Response (DoR) as Assessed by Investigator

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. 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 (up to approximately 8.5 years)

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	176	172		
Units: months				
median (confidence interval 95%)	12.7 (11.1 to 15.5)	32.3 (20.8 to 39.0)		

Statistical analyses

Statistical analysis title	Duration of Response

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	348
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	0.67

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

End point description:

DFS was defined as time from first occurrence of a 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 if present prior to 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. DFS was estimated using Kaplan-Meier method. IRC review was performed up clinical cutoff date of to 1 May 2015. 9999 = non-estimable number due to higher (>50%) number of censored participants.

End point type	Secondary

End point timeframe:

Baseline until PD or death, whichever occurred first (up to approximately 5 years)

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	46		
Units: months				
median (confidence interval 95%)	13.2 (8.5 to 9999)	9999 (9999 to 9999)		

Statistical analyses

Statistical analysis title	Disease Free Survival

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	83
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	0.45

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

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

End point description:

DFS was defined as the time from the first occurrence of a documented CR until progression on the basis of the 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 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. 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. DFS was estimated using Kaplan-Meier method.

End point type	Secondary

End point timeframe:

Baseline until PD or death, whichever occurred first (up to approximately 8.5 years)

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	70		
Units: months				
median (confidence interval 95%)	20.0 (8.6 to 31.0)	36.0 (26.6 to 68.2)		

Statistical analyses

Statistical analysis title	Disease Free Survival

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	120
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	0.81

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

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

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. IRC review was performed up clinical cutoff date of to 1 May 2015.

End point type	Secondary

End point timeframe:

Baseline until PD or death, whichever occurred first (up to approximately 5 years)

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	204		
Units: months				
median (confidence interval 95%)	13.7 (11.4 to 15.5)	25.3 (13.9 to 35.0)		

Statistical analyses

Statistical analysis title	Event-Free Survival

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	413
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	0.44
upper limit	0.74

Secondary: Percentage of Participants Who Died

End point title	Percentage of Participants Who Died

End point description:

End point type	Secondary

End point timeframe:

Baseline until death (up to 8.5 years overall)

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	204		
Units: percentage of participants				
number (not applicable)	49.3	41.2		

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. 9999 = non-estimable number due to higher (>50%) number of censored participants.

End point type	Secondary

End point timeframe:

Baseline until death (up to 8.5 years overall)

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	204		
Units: months				
median (confidence interval 95%)	65.6 (48.5 to 87.8)	88.3 (71.1 to 9999)		

Statistical analyses

Statistical analysis title	Overall Survival

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	413
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.081
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.77

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	1.03

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

End point description:

The 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 ranges from 0-168. Physical Well-being sub-scale includes 7 items measured on 0-4 point scale. The total score for physical well-being sub-scale is sum of each 7 items (range: 0-28). Higher scores indicate a 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) 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).

End point type	Secondary

End point timeframe:

Baseline, Day 1 of Cycles 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, 18 and 24

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	204		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=187, n=187)	22.58 (± 5.23)	22.76 (± 4.61)		
CFB at Cycle 3 Day 1 (n=156, n=154)	-1.56 (± 5.49)	-0.69 (± 4.06)		
CFB at Cycle 4 Day 1 (n=5, n=2)	-6.80 (± 4.21)	-3.00 (± 2.83)		
CFB at Cycle 5 Day 1 (n=142, n=145)	-1.82 (± 5.06)	-0.72 (± 4.16)		
CFB at End of Induction Treatment (n=149, n=142)	-1.00 (± 5.14)	-0.61 (± 4.62)		
CFB at Follow-up Month 2 (n=108, n=133)	0.62 (± 5.14)	0.58 (± 4.45)		
CFB at Follow-up Month 4 (n=95, n=121)	0.53 (± 4.58)	0.88 (± 4.47)		
CFB at Follow-up Month 6 (n=77, n=112)	0.29 (± 3.74)	0.91 (± 3.82)		
CFB at Follow-up Month 8 (n=75, n=104)	-0.01 (± 3.53)	0.87 (± 3.96)		
CFB at Follow-up Month 10 (n=58, n=91)	0.06 (± 4.16)	0.56 (± 3.81)		
CFB at Follow-up Month 12 (n=53, n=90)	0.26 (± 4.02)	0.74 (± 4.24)		
CFB at Follow-up Month 14 (n=46, n=85)	0.03 (± 4.14)	0.71 (± 3.94)		

CFB at Follow-up Month 16 (n=42, n=82)	-0.10 (± 3.49)	1.31 (± 3.68)		
CFB at Follow-up Month 18 (n=41, n=76)	-0.22 (± 3.64)	0.92 (± 3.99)		
CFB at Follow-up Month 20 (n=34, n=73)	-0.36 (± 3.70)	0.74 (± 3.69)		
CFB at Follow-up Month 22 (n=29, n=71)	-0.25 (± 3.93)	0.40 (± 4.47)		
CFB at Follow-up Month 24 (n=30, n=68)	-0.77 (± 4.16)	0.52 (± 4.42)		
CFB at Final Follow-up (n=86, n=106)	0.16 (± 4.17)	0.22 (± 4.47)		
CFB at Extension Follow-up Month 6 (n=21, n=60)	0.36 (± 3.48)	0.57 (± 4.71)		
CFB at Extension Follow-up Month 18 (n=19, n=46)	0.80 (± 2.54)	1.19 (± 4.98)		
CFB at Extension Follow-up Month 24 (n=18, n=39)	1.53 (± 5.96)	0.56 (± 5.26)		

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

End point description:

The 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 ranges from 0-168. Social/family Well-being sub-scale includes 7 items measured on 0-4 point scale. The total score for social/family well-being sub-scale is sum of each 7 items (range: 0-28). 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).

End point type	Secondary

End point timeframe:

Baseline, Day 1 of Cycle 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, 18 and 24

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	204		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=186, n=191)	22.04 (± 5.65)	22.14 (± 5.51)		
CFB at Cycle 3 Day 1 (n=155, n=158)	-0.21 (± 3.59)	-0.10 (± 3.87)		
CFB at Cycle 4 Day 1 (n=5, n=3)	-1.00 (± 3.67)	3.11 (± 2.83)		
CFB at Cycle 5 Day 1 (n=141, n=149)	-0.34 (± 4.32)	-0.34 (± 4.33)		
CFB at End of Induction Treatment (n=147, n=145)	-0.65 (± 5.21)	-0.88 (± 3.60)		

CFB at Follow-up Month 2 (n=106, n=137)	-0.02 (± 4.83)	-0.57 (± 5.37)		
CFB at Follow-up Month 4 (n=94, n=125)	0.27 (± 4.65)	-0.26 (± 5.02)		
CFB at Follow-up Month 6 (n=76, n=114)	0.05 (± 4.46)	-0.08 (± 4.64)		
CFB at Follow-up Month 8 (n=209, n=204)	-0.68 (± 3.67)	-0.37 (± 4.99)		
CFB at Follow-up Month 10 (n=58, n=94)	0.56 (± 5.00)	0.13 (± 5.14)		
CFB at Follow-up Month 12 (n=53, n=93)	0.06 (± 5.89)	-0.47 (± 5.64)		
CFB at Follow-up Month 14 (n=45, n=89)	0.56 (± 3.28)	-0.03 (± 4.16)		
CFB at Follow-up Month 16 (n=42, n=85)	0.36 (± 6.79)	-0.15 (± 5.28)		
CFB at Follow-up Month 18 (n=41, n=78)	0.44 (± 6.23)	0.04 (± 5.35)		
CFB at Follow-up Month 20 (n=34, n=76)	-0.66 (± 4.28)	0.00 (± 5.75)		
CFB at Follow-up Month 22 (n=29, n=74)	0.29 (± 7.12)	-0.50 (± 5.02)		
CFB at Follow-up Month 24 (n=30, n=71)	-1.29 (± 3.91)	-0.41 (± 5.24)		
CFB at Final Follow-up (n=86, n=109)	-0.19 (± 4.91)	-0.52 (± 5.56)		
CFB at Extension Follow-up Month 6 (n=21, n=63)	-0.35 (± 2.49)	-0.16 (± 4.92)		
CFB at Extension Follow-up Month 18 (n=18, n=49)	-0.15 (± 2.92)	0.71 (± 5.26)		
CFB at Extension Follow-up Month 24 (n=18, n=40)	-0.41 (± 3.18)	0.44 (± 5.02)		

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

End point description:

The 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 ranges from 0-168. Emotional Well-being sub-scale includes 6 items measured on 0-4 point scale. The total score for emotional well-being sub-scale is sum of each 6 items (range: 0-24). 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).

End point type	Secondary

End point timeframe:

Baseline, Day 1 of Cycles 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, 18 and 24

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	204		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=189, n=193)	17.38 (± 4.45)	17.81 (± 4.33)		
CFB at Cycle 1 Day 1 (n=0, n=0)	0 (± 0)	0 (± 0)		
CFB at Cycle 3 Day 1 (n=157, n=163)	0.61 (± 3.04)	0.78 (± 3.14)		
CFB at Cycle 4 Day 1 (n=5, n=3)	-0.60 (± 3.85)	3.40 (± 4.42)		
CFB at Cycle 5 Day 1 (n=143, n=152)	0.37 (± 3.08)	0.50 (± 3.52)		
CFB at End of Induction Treatment (n=149, n=145)	0.53 (± 3.57)	0.59 (± 4.03)		
CFB at Follow-up Month 2 (n=107, n=138)	0.66 (± 3.89)	0.67 (± 3.83)		
CFB at Follow-up Month 4 (n=96, n=124)	1.34 (± 3.54)	0.95 (± 3.51)		
CFB at Follow-up Month 6 (n=78, n=116)	0.89 (± 3.57)	0.96 (± 3.44)		
CFB at Follow-up Month 8 (n=76, n=108)	0.26 (± 3.35)	0.97 (± 3.34)		
CFB at Follow-up Month 10 (n=58, n=94)	0.69 (± 3.31)	1.32 (± 3.23)		
CFB at Follow-up Month 12 (n=54, n=93)	-0.07 (± 3.88)	0.95 (± 3.29)		
CFB at Follow-up Month 14 (n=47, n=89)	0.46 (± 3.22)	1.07 (± 3.82)		
CFB at Follow-up Month 16 (n=43, n=86)	0.13 (± 3.87)	1.04 (± 3.69)		
CFB at Follow-up Month 18 (n=41, n=79)	0.42 (± 3.36)	1.00 (± 3.38)		
CFB at Follow-up Month 20 (n=35, n=76)	-0.43 (± 2.90)	0.94 (± 4.28)		
CFB at Follow-up Month 22 (n=30, n=74)	0.18 (± 2.81)	0.97 (± 3.79)		
CFB at Follow-up Month 24 (n=31, n=71)	0.06 (± 3.20)	1.12 (± 3.78)		
CFB at Final Follow-up (n=84, n=111)	0.38 (± 3.77)	0.34 (± 4.37)		
CFB at Extension Follow-up Month 6 (n=23, n=63)	-0.44 (± 3.26)	0.39 (± 3.99)		
CFB at Extension Follow-up Month 18 (n=20, n=50)	-0.08 (± 3.80)	0.75 (± 3.85)		
CFB at Extension Follow-up Month 24 (n=19, n=42)	1.04 (± 4.16)	0.97 (± 4.36)		

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

End point description:

The 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 ranges from 0-168. Functional Well-being sub-scale includes 7 items measured on 0-4 point scale. The total score for functional well-being sub-scale is sum of each 7

items (range: 0-28). 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).

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, 18 and 24

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	204		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=189, n=196)	17.98 (± 6.31)	17.90 (± 6.08)		
CFB at Cycle 1 Day 1 (n=0, n=0)	0 (± 0)	0 (± 0)		
CFB at Cycle 3 Day 1 (n=157, n=165)	-0.54 (± 4.65)	0.38 (± 4.66)		
CFB at Cycle 4 Day 1 (n=5, n=3)	-0.80 (± 2.28)	1.78 (± 4.91)		
CFB at Cycle 5 Day 1 (n=143, n=154)	-0.71 (± 5.04)	0.67 (± 5.35)		
CFB at End of Induction Treatment (n=150, n=147)	-0.50 (± 5.50)	0.00 (± 5.25)		
CFB at Follow-up Month 2 (n=107, n=139)	0.31 (± 5.27)	0.65 (± 5.38)		
CFB at Follow-up Month 4 (n=96, n=126)	0.24 (± 5.11)	1.31 (± 5.86)		
CFB at Follow-up Month 6 (n=77, n=117)	0.95 (± 4.58)	1.26 (± 5.08)		
CFB at Follow-up Month 8 (n=76, n=109)	-0.27 (± 4.38)	0.92 (± 5.45)		
CFB at Follow-up Month 10 (n=59, n=96)	1.09 (± 4.25)	1.00 (± 5.52)		
CFB at Follow-up Month 12 (n=54, n=94)	0.18 (± 5.59)	1.78 (± 6.04)		
CFB at Follow-up Month 14 (n=47, n=90)	1.16 (± 4.27)	1.22 (± 4.84)		
CFB at Follow-up Month 16 (n=43, n=87)	0.91 (± 3.97)	1.69 (± 5.95)		
CFB at Follow-up Month 18 (n=41, n=79)	0.21 (± 4.12)	1.84 (± 5.77)		
CFB at Follow-up Month 20 (n=35, n=77)	-0.27 (± 4.90)	1.43 (± 6.14)		
CFB at Follow-up Month 22 (n=30, n=75)	-0.32 (± 5.70)	0.82 (± 5.00)		
CFB at Follow-up Month 24 (n=31, n=71)	-0.96 (± 4.36)	0.98 (± 5.87)		
CFB at Final Follow-up (n=84, n=114)	-0.08 (± 4.94)	0.50 (± 6.19)		
CFB at Extension Follow-up Month 6 (n=23, n=63)	1.01 (± 3.51)	0.85 (± 6.65)		
CFB at Extension Follow-up Month 18 (n=19, n=50)	0.96 (± 4.51)	1.90 (± 6.50)		
CFB at Extension Follow-up Month 24 (n=19, n=42)	2.22 (± 3.34)	2.62 (± 6.95)		

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

End point description:

The 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 ranges from 0-168. Lymphoma scale includes 15 items measured on 0-4 point scale. The total score for lymphoma sub-scale is sum of each 15 items (range: 0-60). 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). 9999 = non-applicable number

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, 18 and 24

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	204		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=189, n=194)	44.79 (± 9.66)	45.61 (± 9.17)		
CFB at Cycle 1 Day 1 (n=209, n=204)	9999 (± 9999)	9999 (± 9999)		
CFB at Cycle 3 Day 1 (n=154, n=162)	0.98 (± 6.97)	1.24 (± 5.71)		
CFB at Cycle 4 Day 1 (n=5, n=2)	-2.80 (± 5.76)	9.50 (± 3.54)		
CFB at Cycle 5 Day 1 (n=142, n=151)	0.75 (± 6.79)	1.41 (± 6.21)		
CFB at End of Induction Treatment (n=148, n=148)	1.64 (± 7.10)	0.74 (± 7.89)		
CFB at Follow-up Month 2 (n=107, n=135)	3.44 (± 6.78)	2.45 (± 6.22)		
CFB at Follow-up Month 4 (n=96, n=123)	2.77 (± 6.71)	2.39 (± 6.54)		
CFB at Follow-up Month 6 (n=79, n=117)	2.33 (± 6.44)	3.00 (± 7.05)		
CFB at Follow-up Month 8 (n=75, n=107)	1.79 (± 6.01)	2.52 (± 6.69)		
CFB at Follow-up Month 10 (n=59 n=94)	1.90 (± 6.78)	2.28 (± 6.82)		
CFB at Follow-up Month 12 (n=53, n=94)	2.12 (± 6.47)	2.89 (± 6.42)		
CFB at Follow-up Month 14 (n=47, n=91)	0.48 (± 6.64)	2.58 (± 6.37)		

CFB at Follow-up Month 16 (n=42, n=86)	0.44 (± 7.79)	3.27 (± 6.14)		
CFB at Follow-up Month 18 (n=42, n=78)	1.18 (± 6.09)	2.91 (± 6.79)		
CFB at Follow-up Month 20 (n=34, n=75)	0.57 (± 7.43)	2.83 (± 6.41)		
CFB at Follow-up Month 22 (n=30, n=72)	1.89 (± 8.62)	2.55 (± 6.58)		
CFB at Follow-up Month 24 (n=31, n=70)	0.66 (± 7.59)	2.73 (± 6.48)		
CFB at Final Follow-up (n=85, n=112)	1.62 (± 7.17)	1.33 (± 7.38)		
CFB at Extension Follow-up Month 6 (n=23, n=61)	0.92 (± 5.06)	2.98 (± 7.22)		
CFB at Extension Follow-up Month 18 (n=20, n=50)	1.80 (± 8.30)	2.35 (± 5.72)		
CFB at Extension Follow-up Month 24 (n=19, n=42)	4.89 (± 6.67)	2.23 (± 6.85)		

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

End point description:

EQ-5D: participant rated questionnaire to assess health-related quality of life in terms of a single utility score; assesses level of current health for 5 domains: mobility, self-care, usual activities, pain and discomfort, and anxiety and depression; 1 indicates better health state (no problems); 3 indicates worst health state ("confined to bed"). Score is transformed and results in a total score range -0.594 to 1.000; higher score indicates a 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. 9999 = non-applicable number.

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 and 14

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	204		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=186, 193)	0.77 (± 0.22)	0.79 (± 0.20)		
CFB at Cycle 3 Day 1 (n=157, 161)	0.03 (± 0.21)	0.00 (± 0.19)		
CFB at Cycle 4 Day 1 (n=5, 3)	-0.10 (± 0.23)	-0.07 (± 0.41)		
CFB at Cycle 5 Day 1 (n=142, 153)	0.01 (± 0.21)	0.02 (± 0.20)		

CFB at End of Induction Treatment (n=136, 140)	0.01 (± 0.22)	0.01 (± 0.20)		
CFB at Follow-up Month 2 (n=39, 135)	0.06 (± 0.24)	0.04 (± 0.18)		
CFB at Follow-up Month 4 (n=0, 2)	9999 (± 9999)	-0.12 (± 0.00)		
CFB at Follow-up Month 14 (n=1, 0)	0.12 (± 9999)	9999 (± 9999)		

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

End point description:

EQ-5D: participant rated questionnaire to assess health-related quality of life in terms of a single utility score. Health State Profile component assesses level of current health for 5 domains: mobility, self-care, usual activities, pain and discomfort, and anxiety and depression; 1 indicates better health state (no problems); 3 indicates worst health state ("confined to bed"). Scoring formula developed by EuroQoL Group assigns a utility value for each domain in the profile. Score is transformed and results in a total score range -0.594 to 1.000; higher score indicates 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.

End point type	Secondary

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)

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	158		
Units: units on a scale				
arithmetic mean (standard deviation)				
CFB at Follow-up Month 2 (n=0, 2)	9999 (± 9999)	-0.15 (± 0.22)		
CFB at Follow-up Month 4 (n= 1, 119)	0.15 (± 9999)	0.03 (± 0.22)		
CFB at Follow-up Month 6 (n= 1, 109)	0.15 (± 9999)	0.04 (± 0.19)		
CFB at Follow-up Month 8 (n= 1, 101)	0.15 (± 9999)	0.04 (± 0.21)		
CFB at Follow-up Month 10 (n= 1, 91)	0.15 (± 9999)	0.03 (± 0.20)		
CFB at Follow-up Month 12 (n= 0, 87)	9999 (± 9999)	0.06 (± 0.18)		
CFB at Follow-up Month 14 (n= 0, 80)	9999 (± 9999)	0.06 (± 0.19)		
CFB at Follow-up Month 16 (n= 0, 78)	9999 (± 9999)	0.05 (± 0.19)		
CFB at Follow-up Month 18 (n= 0, 73)	9999 (± 9999)	0.05 (± 0.18)		
CFB at Follow-up Month 20 (n= 0, 69)	9999 (± 9999)	0.05 (± 0.20)		
CFB at Follow-up Month 22 (n= 0, 69)	9999 (± 9999)	0.05 (± 0.24)		
CFB at Follow-up Month 24 (n= 0, 64)	9999 (± 9999)	0.03 (± 0.22)		
CFB at Final Follow-up (n= 0, 39)	9999 (± 9999)	0.03 (± 0.25)		

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

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 millimeter (mm) (worst imaginable health state) to 100 mm (best imaginable health state); higher scores indicate a 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. 9999 = non-applicable number

End point type	Secondary

End point timeframe:

Baseline, Day 1 of Cycles 3, 4, 5, End of induction treatment (up to Month 6); Follow-up Months 2, 4 and 14

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	204		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=183, 188)	69.48 (± 20.71)	68.03 (± 21.69)		
CFB at Cycle 3 Day 1 (n=152, 153)	0.91 (± 19.38)	3.32 (± 15.99)		
CFB at Cycle 4 Day 1 (n=5, 3)	-14.00 (± 33.29)	-4.33 (± 42.15)		
CFB at Cycle 5 Day 1 (n=136, 141)	0.35 (± 20.79)	5.17 (± 17.35)		
CFB at End of Induction Treatment (n=132, 135)	5.71 (± 61.88)	5.82 (± 22.20)		
CFB at Follow-up Month 2 (n=36, 128)	5.19 (± 19.12)	6.85 (± 18.95)		
CFB at Follow-up Month 4 (n=0, 2)	9999 (± 9999)	0.00 (± 14.14)		
CFB at Follow-up Month 14 (n=1, 0)	10.00 (± 9999)	9999 (± 9999)		

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

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. 9999 = non-calculable number

End point type	Secondary

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)

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	158		
Units: units on a scale				
arithmetic mean (standard deviation)				
CFB at Follow-up Month 2 (n= 0, 1)	9999 (± 9999)	-40.00 (± 9999)		
CFB at Follow-up Month 4 (n= 1, 111)	5.00 (± 9999)	5.59 (± 19.61)		
CFB at Follow-up Month 6 (n= 1, 106)	5.00 (± 9999)	6.04 (± 19.00)		
CFB at Follow-up Month 8 (n= 1, 95)	5.00 (± 9999)	4.79 (± 17.18)		
CFB at Follow-up Month 10 (n= 1, 86)	-15.00 (± 9999)	4.62 (± 16.28)		
CFB at Follow-up Month 12 (n= 0, 82)	9999 (± 9999)	5.73 (± 16.04)		
CFB at Follow-up Month 14 (n= 0, 77)	9999 (± 9999)	5.45 (± 17.36)		
CFB at Follow-up Month 16 (n= 0, 76)	9999 (± 9999)	6.66 (± 17.44)		
CFB at Follow-up Month 18 (n= 0, 69)	9999 (± 9999)	6.13 (± 19.44)		
CFB at Follow-up Month 20 (n=0, 66)	9999 (± 9999)	7.56 (± 15.43)		
CFB at Follow-up Month 22 (n= 0, 64)	9999 (± 9999)	6.97 (± 15.55)		
CFB at Follow-up Month 24 (n= 0, 61)	9999 (± 9999)	8.28 (± 16.23)		
CFB at Final Follow-up (n= 0, 38)	9999 (± 9999)	4.47 (± 14.91)		

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

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).

End point type	Secondary

End point timeframe:

Baseline, Day 1 of Cycles 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, 18 and 24

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	204		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=185, n=186)	79.86 (± 16.25)	80.78 (± 16.27)		
CFB at Cycle 3 Day 1 (n=154, n=154)	-1.87 (± 12.28)	0.11 (± 10.30)		
CFB at Cycle 4 Day 1 (n=5, n=2)	-9.37 (± 9.89)	0.52 (± 4.98)		
CFB at Cycle 5 Day 1 (n=140, n=145)	-2.44 (± 12.01)	0.06 (± 11.13)		
CFB at End of Induction Treatment (n=146, n=140)	-1.84 (± 13.83)	-0.92 (± 11.77)		
CFB at Follow-up Month 2 (n=107, n=133)	1.53 (± 13.42)	1.22 (± 12.01)		
CFB at Follow-up Month 4 (n=95, n=120)	2.55 (± 11.47)	3.06 (± 13.00)		
CFB at Follow-up Month 6 (n=75, n=111)	2.54 (± 10.68)	3.24 (± 11.40)		
CFB at Follow-up Month 8 (n=74, n=104)	-0.53 (± 10.15)	2.49 (± 11.45)		
CFB at Follow-up Month 10 (n=57, n=88)	2.29 (± 11.39)	3.46 (± 11.83)		
CFB at Follow-up Month 12 (n=53, n=90)	0.68 (± 13.16)	2.82 (± 14.29)		
CFB at Follow-up Month 14 (n=45, n=84)	2.48 (± 9.42)	2.94 (± 11.97)		
CFB at Follow-up Month 16 (n=42, n=82)	1.54 (± 10.61)	4.09 (± 12.87)		
CFB at Follow-up Month 18 (n=39, n=76)	1.16 (± 11.57)	4.06 (± 13.36)		
CFB at Follow-up Month 20 (n=33, n=73)	-1.21 (± 12.25)	3.05 (± 14.29)		
CFB at Follow-up Month 22 (n=28, n=71)	0.64 (± 14.27)	1.80 (± 12.43)		
CFB at Follow-up Month 24 (n=29, n=67)	-2.39 (± 9.32)	2.28 (± 13.83)		
CFB at Final Follow-up (n=84, n=106)	0.50 (± 11.25)	0.78 (± 14.94)		
CFB at Extension Follow Up Month 6 (n=21, n=60)	0.48 (± 8.71)	1.74 (± 14.23)		
CFB at Extension Follow Up Month 18 (n=18, n=46)	2.29 (± 8.40)	4.56 (± 15.02)		
CFB at Extension Follow Up Month 24 (n=18, n=38)	4.48 (± 11.10)	4.47 (± 15.22)		

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)

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).

End point type	Secondary

End point timeframe:

Baseline, Day 1 of Cycles 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, 18 and 24

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	204		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=190, n=196)	84.66 (± 19.36)	84.76 (± 18.97)		
CFB at Cycle 3 Day 1 (n=159, n=165)	-1.94 (± 17.96)	1.81 (± 13.88)		
CFB at Cycle 4 Day 1 (n=5, n=3)	-10.40 (± 10.38)	26.44 (± 19.51)		
CFB at Cycle 5 Day 1 (n=144, n=154)	-1.38 (± 15.38)	2.37 (± 14.15)		
CFB at End of Induction Treatment (n=151, n=149)	-0.52 (± 17.23)	0.40 (± 16.45)		
CFB at Follow-up Month 2 (n=108, n=139)	3.75 (± 15.36)	4.60 (± 14.85)		
CFB at Follow-up Month 4 (n=96, n=127)	3.81 (± 13.39)	5.18 (± 17.06)		
CFB at Follow-up Month 6 (n=79, n=117)	3.26 (± 12.19)	6.07 (± 13.72)		
CFB at Follow-up Month 8 (n=76, n=109)	1.36 (± 12.39)	5.36 (± 14.21)		
CFB at Follow-up Month 10 (n=59, n=96)	3.52 (± 13.16)	4.94 (± 15.96)		
CFB at Follow-up Month 12 (n=54, n=95)	2.05 (± 15.14)	6.13 (± 15.72)		

CFB at Follow-up Month 14 (n=47, n=91)	2.25 (± 11.92)	5.13 (± 14.30)		
CFB at Follow-up Month 16 (n=43, n=87)	0.75 (± 14.15)	6.78 (± 15.11)		
CFB at Follow-up Month 18 (n=42, n=79)	1.36 (± 11.30)	7.26 (± 14.62)		
CFB at Follow-up Month 20 (n=35, n=77)	-0.64 (± 15.21)	6.36 (± 14.99)		
CFB at Follow-up Month 22 (n=30, n=75)	2.26 (± 14.54)	5.30 (± 17.88)		
CFB at Follow-up Month 24 (n=31, n=72)	-0.14 (± 13.44)	5.30 (± 17.88)		
CFB at Final Follow-up (n=86, n=114)	0.84 (± 14.80)	3.84 (± 16.22)		
CFB at Extension Follow Up Month 6 (n=23, n=63)	2.30 (± 10.77)	5.53 (± 18.44)		
CFB at Extension Follow Up Month 18 (n=20, n=50)	4.02 (± 14.01)	7.31 (± 15.69)		
CFB at Extension Follow Up Month 24 (n=19, n=42)	10.04 (± 13.35)	7.07 (± 17.59)		

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

End point description:

FACT-Lym total score is the 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 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).

End point type	Secondary

End point timeframe:

Baseline, Day 1 of Cycles 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, 18 and 24

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	204		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=186, n=187)	124.56 (± 24.17)	126.22 (± 23.98)		
CFB at Cycle 3 Day 1 (n=153, n=154)	-0.74 (± 17.91)	1.33 (± 13.89)		
CFB at Cycle 4 Day 1 (n=5, n=2)	-12.16 (± 14.80)	22.53 (± 16.23)		

CFB at Cycle 5 Day 1 (n=140, n=144)	-1.68 (± 16.61)	1.71 (± 15.23)		
CFB at End of Induction Treatment (n=147, n=140)	0.02 (± 18.55)	0.35 (± 18.29)		
CFB at Follow-up Month 2 (n=106, n=131)	5.10 (± 17.73)	3.54 (± 15.45)		
CFB at Follow-up Month 4 (n=95, n=119)	5.40 (± 16.29)	5.50 (± 17.76)		
CFB at Follow-up Month 6 (n=76, n=113)	5.03 (± 15.01)	6.57 (± 15.96)		
CFB at Follow-up Month 8 (n=74, n=104)	1.48 (± 14.27)	5.18 (± 15.61)		
CFB at Follow-up Month 10 (n=58, n=91)	4.58 (± 16.39)	5.70 (± 16.89)		
CFB at Follow-up Month 12 (n=52, n=91)	2.97 (± 17.84)	5.88 (± 18.93)		
CFB at Follow-up Month 14 (n=45, n=87)	3.18 (± 13.85)	5.92 (± 17.06)		
CFB at Follow-up Month 16 (n=41, n=83)	2.25 (± 14.98)	7.59 (± 16.97)		
CFB at Follow-up Month 18 (n=40, n=76)	2.16 (± 15.38)	6.99 (± 18.27)		
CFB at Follow-up Month 20 (n=33, n=73)	-0.89 (± 16.34)	5.66 (± 18.90)		
CFB at Follow-up Month 22 (n=29, n=71)	2.15 (± 19.03)	4.59 (± 17.98)		
CFB at Follow-up Month 24 (n=30, n=67)	-2.13 (± 15.74)	5.28 (± 18.75)		
CFB at Final follow-up (n=84, n=105)	2.15 (± 16.60)	2.55 (± 20.11)		
CFB at Extension Follow Up Month 6 (n=21, n=60)	1.22 (± 11.67)	5.14 (± 20.30)		
CFB at Extension Follow Up Month 18 (n=18, n=48)	4.92 (± 14.73)	6.88 (± 19.24)		
CFB at Extension Follow Up Month 24 (n=18, n=41)	9.69 (± 15.88)	6.13 (± 20.32)		

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

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 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).

End point type	Secondary

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	209	204		
Units: Months				
median (confidence interval 95%)	5.6 (3.9 to 7.0)	8.0 (5.9 to 14.7)		

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

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).

End point type	Secondary

End point timeframe:

Baseline, Cycle 5 Day 1 (C5D1) (Cycle length = 28 days), Follow-up Months 6 (FUM6), 12 (FUM12), 18 (FUM18), 24 (FUM24), Extension Follow Up Month 6 (Ext FUM6)

End point values	Bendamustine alone	Obinutuzumab + Bendamustine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	204		
Units: Percentage of participants				
number (not applicable)				
C5D1 (n=155, n=156) (>=3 pt increase)	30.3	41.7		
FUM6 (n=87, n=119) (>=3 pt increase)	37.9	47.1		
FUM12 (n=60, n=99) (>=3 pt increase)	36.7	46.5		
FUM18 (n=45, n=83) (>=3 pt increase)	35.6	53.0		
FUM24 (n=34, n=74) (>=3 pt increase)	35.3	50		
Ext FUM6 (n=25, n=64) (>=3 pt increase)	36.0	57.8		
C5D1 (n=156, n=157) (>=6 pt increase)	23.1	34.4		

FUM6 (n=88, n=119) (>=6 pt increase)	29.5	43.7		
FUM12 (n=61, n=100) (>=6 pt increase)	26.2	47.0		
FUM18 (n=45, n=83) (>=6 pt increase)	28.9	51.8		
FUM24 (n=34, n=74) (>=6 pt increase)	26.5	48.0		
Ext FUM6 (n=25, n=64) (>=6 pt increase)	44	56.9		
C5D1 (n=156, n=157) (>=7 pt increase)	24.4	28.0		
FUM6 (n=88, n=119) (>=7 pt increase)	34.1	40.3		
FUM12 (n=61, n=100) (>=7 pt increase)	31.1	45.0		
FUM18 (n=45, n=83) (>=7 pt increase)	31.1	43.4		
FUM24 (n=34, n=75) (>=7 pt increase)	20.6	42.7		
Ext FUM6 (n=25, n=65) (>=7 pt increase)	32	47.7		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 8.5 years

Adverse event reporting additional description:

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Bendamustine alone

Reporting group description:

Participants received Bendamustine 120 mg/m^2 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 CR, PR or SD then received obinutuzumab 1000 mg IV infusion every 2 months until disease progression or for up to 2 years (whichever occurred first).

Serious adverse events	Bendamustine alone	Obinutuzumab + Bendamustine	
Total subjects affected by serious adverse events			
subjects affected / exposed	76 / 203 (37.44%)	91 / 204 (44.61%)	
number of deaths (all causes)	100	84	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ACUTE MYELOID LEUKAEMIA			
subjects affected / exposed	2 / 203 (0.99%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	2 / 2	1 / 1	
ADENOCARCINOMA			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
ADENOCARCINOMA GASTRIC			

subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
BASAL CELL CARCINOMA			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLADDER CANCER			
subjects affected / exposed	0 / 203 (0.00%)	2 / 204 (0.98%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
BREAST CANCER			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRONCHIAL NEOPLASM			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHOLANGIOCARCINOMA			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COLORECTAL CANCER			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
INTESTINAL ADENOCARCINOMA			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
LEIOMYOSARCOMA			

subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEUKAEMIA			
subjects affected / exposed	2 / 203 (0.99%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
LUNG NEOPLASM MALIGNANT			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MALIGNANT MELANOMA			
subjects affected / exposed	1 / 203 (0.49%)	2 / 204 (0.98%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
MYELODYSPLASTIC SYNDROME			
subjects affected / exposed	1 / 203 (0.49%)	3 / 204 (1.47%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	1 / 1	
POLYCYTHAEMIA VERA			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL CANCER			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SQUAMOUS CELL CARCINOMA			
subjects affected / exposed	3 / 203 (1.48%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
T-CELL LYMPHOMA			

subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
THYROID NEOPLASM			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
CIRCULATORY COLLAPSE			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
DEEP VEIN THROMBOSIS			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOTENSION			
subjects affected / exposed	2 / 203 (0.99%)	2 / 204 (0.98%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
CATHETER SITE PAIN			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHEST PAIN			
subjects affected / exposed	2 / 203 (0.99%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
FATIGUE			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	0 / 203 (0.00%)	3 / 204 (1.47%)	
occurrences causally related to treatment / all	0 / 0	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERTHERMIA			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MALAISE			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PYREXIA			
subjects affected / exposed	3 / 203 (1.48%)	6 / 204 (2.94%)	
occurrences causally related to treatment / all	1 / 3	2 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
GRAFT VERSUS HOST DISEASE			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Social circumstances			
SOCIAL PROBLEM			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
BENIGN PROSTATIC HYPERPLASIA			

subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
BRONCHOSPASM			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHYLOTHORAX			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
EMPHYSEMA			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOXIA			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PLEURAL EFFUSION			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA ASPIRATION			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMOTHORAX			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY EMBOLISM			

subjects affected / exposed	3 / 203 (1.48%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MANIA			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BORRELIA TEST			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (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	0 / 203 (0.00%)	2 / 204 (0.98%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEAD INJURY			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HIP FRACTURE			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

INFUSION RELATED REACTION			
subjects affected / exposed	3 / 203 (1.48%)	7 / 204 (3.43%)	
occurrences causally related to treatment / all	3 / 3	7 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
JAW FRACTURE			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
POST PROCEDURAL BILE LEAK			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEROMA			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
STAB WOUND			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VASCULAR PSEUDOANEURYSM			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
WRIST FRACTURE			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
HYDROCELE			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (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	1 / 203 (0.49%)	2 / 204 (0.98%)	
occurrences causally related to treatment / all	2 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIAL FLUTTER			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC FAILURE			
subjects affected / exposed	0 / 203 (0.00%)	2 / 204 (0.98%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
CORONARY ARTERY DISEASE			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYOCARDIAL INFARCTION			
subjects affected / exposed	1 / 203 (0.49%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
PAROXYSMAL ARRHYTHMIA			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
AMYOTROPHIC LATERAL SCLEROSIS			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
CENTRAL NERVOUS SYSTEM LESION			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

HEADACHE			
subjects affected / exposed	1 / 203 (0.49%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ISCHAEMIC STROKE			
subjects affected / exposed	2 / 203 (0.99%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
POST HERPETIC NEURALGIA			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PRESYNCOPE			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUBARACHNOID HAEMORRHAGE			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SYNCOPE			
subjects affected / exposed	0 / 203 (0.00%)	2 / 204 (0.98%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
AGRANULOCYTOSIS			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
ANAEMIA			
subjects affected / exposed	3 / 203 (1.48%)	3 / 204 (1.47%)	
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	6 / 203 (2.96%)	11 / 204 (5.39%)	
occurrences causally related to treatment / all	6 / 6	16 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEUKOPENIA			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPENIA			
subjects affected / exposed	1 / 203 (0.49%)	6 / 204 (2.94%)	
occurrences causally related to treatment / all	1 / 1	5 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
THROMBOCYTOPENIA			
subjects affected / exposed	0 / 203 (0.00%)	5 / 204 (2.45%)	
occurrences causally related to treatment / all	0 / 0	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
NECROTISING RETINITIS			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
ABDOMINAL PAIN UPPER			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANAL FISSURE			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COLITIS			
subjects affected / exposed	0 / 203 (0.00%)	2 / 204 (0.98%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA			

subjects affected / exposed	3 / 203 (1.48%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FOOD POISONING			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMATOCHEZIA			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTESTINAL PERFORATION			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LARGE INTESTINAL OBSTRUCTION			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MELAENA			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NAUSEA			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCREATITIS			

subjects affected / exposed	0 / 203 (0.00%)	2 / 204 (0.98%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
RECTAL HAEMORRHAGE			
subjects affected / exposed	0 / 203 (0.00%)	2 / 204 (0.98%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
UPPER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VOMITING			
subjects affected / exposed	1 / 203 (0.49%)	2 / 204 (0.98%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
CHOLECYSTITIS			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
PARANEOPLASTIC PEMPHIGUS			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
DYSURIA			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
END STAGE RENAL DISEASE			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

HAEMATURIA			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
POLLAKIURIA			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
URETERIC OBSTRUCTION			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY INCONTINENCE			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
MUSCLE HAEMORRHAGE			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
OSTEOARTHRITIS			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
ATYPICAL PNEUMONIA			
subjects affected / exposed	1 / 203 (0.49%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BACTERAEMIA			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

BRONCHITIS			
subjects affected / exposed	3 / 203 (1.48%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	1 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CAMPYLOBACTER INFECTION			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COXSACKIE MYOCARDITIS			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
DEVICE RELATED SEPSIS			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENCEPHALITIS VIRAL			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENDOCARDITIS			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ERYSIPELAS			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ESCHERICHIA SEPSIS			
subjects affected / exposed	0 / 203 (0.00%)	2 / 204 (0.98%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
FUNGAL SEPSIS			

subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
GASTROENTERITIS			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
GASTROENTERITIS NOROVIRUS			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATITIS B REACTIVATION			
subjects affected / exposed	1 / 203 (0.49%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HERPES ZOSTER			
subjects affected / exposed	3 / 203 (1.48%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	3 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTION			
subjects affected / exposed	2 / 203 (0.99%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 203 (0.49%)	3 / 204 (1.47%)	
occurrences causally related to treatment / all	0 / 5	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUNG INFECTION			
subjects affected / exposed	1 / 203 (0.49%)	2 / 204 (0.98%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUNG INFECTION PSEUDOMONAL			

subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPENIC SEPSIS			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
PNEUMOCYSTIS JIROVECII PNEUMONIA			
subjects affected / exposed	2 / 203 (0.99%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	2 / 2	0 / 0	
PNEUMONIA			
subjects affected / exposed	12 / 203 (5.91%)	7 / 204 (3.43%)	
occurrences causally related to treatment / all	6 / 12	2 / 7	
deaths causally related to treatment / all	0 / 1	0 / 0	
PNEUMONIA CYTOMEGALOVIRAL			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PSEUDOMONAL SEPSIS			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
PSEUDOMONAS BRONCHITIS			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY SYNCYTIAL VIRUS INFECTION			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY TRACT INFECTION			

subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPSIS			
subjects affected / exposed	7 / 203 (3.45%)	6 / 204 (2.94%)	
occurrences causally related to treatment / all	4 / 7	3 / 6	
deaths causally related to treatment / all	1 / 3	0 / 1	
SEPTIC SHOCK			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SINUSITIS			
subjects affected / exposed	1 / 203 (0.49%)	2 / 204 (0.98%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
STAPHYLOCOCCAL SEPSIS			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
TOOTH INFECTION			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 203 (0.49%)	2 / 204 (0.98%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 203 (0.00%)	3 / 204 (1.47%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
UROSEPSIS			

subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VASCULAR DEVICE INFECTION			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	2 / 203 (0.99%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOKALAEMIA			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TUMOUR LYSIS SYNDROME			
subjects affected / exposed	2 / 203 (0.99%)	0 / 204 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

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

Non-serious adverse events	Bendamustine alone	Obinutuzumab + Bendamustine	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	194 / 203 (95.57%)	200 / 204 (98.04%)	
Vascular disorders			
HYPOTENSION			
subjects affected / exposed	1 / 203 (0.49%)	23 / 204 (11.27%)	
occurrences (all)	2	26	

PHLEBITIS			
subjects affected / exposed	13 / 203 (6.40%)	11 / 204 (5.39%)	
occurrences (all)	14	11	
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	25 / 203 (12.32%)	31 / 204 (15.20%)	
occurrences (all)	35	44	
CHEST PAIN			
subjects affected / exposed	4 / 203 (1.97%)	11 / 204 (5.39%)	
occurrences (all)	4	11	
CHILLS			
subjects affected / exposed	21 / 203 (10.34%)	28 / 204 (13.73%)	
occurrences (all)	24	30	
FATIGUE			
subjects affected / exposed	67 / 203 (33.00%)	81 / 204 (39.71%)	
occurrences (all)	114	151	
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	9 / 203 (4.43%)	11 / 204 (5.39%)	
occurrences (all)	10	12	
MUCOSAL INFLAMMATION			
subjects affected / exposed	8 / 203 (3.94%)	11 / 204 (5.39%)	
occurrences (all)	11	12	
OEDEMA PERIPHERAL			
subjects affected / exposed	14 / 203 (6.90%)	15 / 204 (7.35%)	
occurrences (all)	17	16	
PYREXIA			
subjects affected / exposed	36 / 203 (17.73%)	54 / 204 (26.47%)	
occurrences (all)	44	80	
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	40 / 203 (19.70%)	64 / 204 (31.37%)	
occurrences (all)	46	85	
DYSPNOEA			
subjects affected / exposed	23 / 203 (11.33%)	26 / 204 (12.75%)	
occurrences (all)	28	27	
NASAL CONGESTION			

subjects affected / exposed	5 / 203 (2.46%)	17 / 204 (8.33%)	
occurrences (all)	6	18	
OROPHARYNGEAL PAIN			
subjects affected / exposed	7 / 203 (3.45%)	12 / 204 (5.88%)	
occurrences (all)	7	15	
RHINORRHOEA			
subjects affected / exposed	3 / 203 (1.48%)	11 / 204 (5.39%)	
occurrences (all)	3	11	
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	21 / 203 (10.34%)	21 / 204 (10.29%)	
occurrences (all)	26	24	
Investigations			
WEIGHT DECREASED			
subjects affected / exposed	18 / 203 (8.87%)	11 / 204 (5.39%)	
occurrences (all)	18	11	
Injury, poisoning and procedural complications			
INFUSION RELATED REACTION			
subjects affected / exposed	115 / 203 (56.65%)	125 / 204 (61.27%)	
occurrences (all)	242	283	
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	17 / 203 (8.37%)	14 / 204 (6.86%)	
occurrences (all)	23	22	
DYSGEUSIA			
subjects affected / exposed	16 / 203 (7.88%)	15 / 204 (7.35%)	
occurrences (all)	20	20	
HEADACHE			
subjects affected / exposed	32 / 203 (15.76%)	27 / 204 (13.24%)	
occurrences (all)	37	36	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	34 / 203 (16.75%)	23 / 204 (11.27%)	
occurrences (all)	41	36	
NEUTROPENIA			

subjects affected / exposed	59 / 203 (29.06%)	74 / 204 (36.27%)	
occurrences (all)	103	150	
THROMBOCYTOPENIA			
subjects affected / exposed	50 / 203 (24.63%)	26 / 204 (12.75%)	
occurrences (all)	101	54	
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	11 / 203 (5.42%)	6 / 204 (2.94%)	
occurrences (all)	12	6	
ABDOMINAL PAIN			
subjects affected / exposed	20 / 203 (9.85%)	16 / 204 (7.84%)	
occurrences (all)	23	18	
ABDOMINAL PAIN UPPER			
subjects affected / exposed	15 / 203 (7.39%)	11 / 204 (5.39%)	
occurrences (all)	19	12	
CONSTIPATION			
subjects affected / exposed	40 / 203 (19.70%)	42 / 204 (20.59%)	
occurrences (all)	55	56	
DIARRHOEA			
subjects affected / exposed	61 / 203 (30.05%)	57 / 204 (27.94%)	
occurrences (all)	83	81	
DRY MOUTH			
subjects affected / exposed	12 / 203 (5.91%)	8 / 204 (3.92%)	
occurrences (all)	15	8	
DYSPEPSIA			
subjects affected / exposed	9 / 203 (4.43%)	13 / 204 (6.37%)	
occurrences (all)	11	16	
NAUSEA			
subjects affected / exposed	123 / 203 (60.59%)	107 / 204 (52.45%)	
occurrences (all)	227	210	
VOMITING			
subjects affected / exposed	54 / 203 (26.60%)	44 / 204 (21.57%)	
occurrences (all)	87	67	
Skin and subcutaneous tissue disorders			
PRURITUS			

subjects affected / exposed	12 / 203 (5.91%)	29 / 204 (14.22%)	
occurrences (all)	13	38	
RASH			
subjects affected / exposed	24 / 203 (11.82%)	28 / 204 (13.73%)	
occurrences (all)	27	35	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	11 / 203 (5.42%)	24 / 204 (11.76%)	
occurrences (all)	12	31	
BACK PAIN			
subjects affected / exposed	18 / 203 (8.87%)	17 / 204 (8.33%)	
occurrences (all)	22	19	
MYALGIA			
subjects affected / exposed	15 / 203 (7.39%)	13 / 204 (6.37%)	
occurrences (all)	17	14	
PAIN IN EXTREMITY			
subjects affected / exposed	10 / 203 (4.93%)	22 / 204 (10.78%)	
occurrences (all)	13	27	
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	18 / 203 (8.87%)	24 / 204 (11.76%)	
occurrences (all)	23	36	
HERPES ZOSTER			
subjects affected / exposed	14 / 203 (6.90%)	10 / 204 (4.90%)	
occurrences (all)	16	10	
NASOPHARYNGITIS			
subjects affected / exposed	8 / 203 (3.94%)	22 / 204 (10.78%)	
occurrences (all)	10	27	
RHINITIS			
subjects affected / exposed	8 / 203 (3.94%)	12 / 204 (5.88%)	
occurrences (all)	9	13	
SINUSITIS			
subjects affected / exposed	11 / 203 (5.42%)	24 / 204 (11.76%)	
occurrences (all)	14	35	
UPPER RESPIRATORY TRACT INFECTION			

subjects affected / exposed	17 / 203 (8.37%)	26 / 204 (12.75%)	
occurrences (all)	21	34	
URINARY TRACT INFECTION			
subjects affected / exposed	12 / 203 (5.91%)	23 / 204 (11.27%)	
occurrences (all)	14	36	
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	37 / 203 (18.23%)	37 / 204 (18.14%)	
occurrences (all)	49	40	
HYPOKALAEMIA			
subjects affected / exposed	15 / 203 (7.39%)	15 / 204 (7.35%)	
occurrences (all)	21	22	

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 modifid 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).
23 August 2017	A specific section for non-serious Adverse Events of Special Interest (AESIs) was added to align with reporting rules for other obinutuzumab/Gazyva/Gazyvaro protocols. The study was amended to consider second malignancies as an AESI and to report these events indefinitely, regardless of relationship to study treatment. The reporting requirements were amended to collect full information about the extent of events of second malignancies in real time. The protocol was modified to prohibit use of the term "sudden death" on the Adverse Event electronic Case Report Form (eCRF), unless it is combined with the presumed cause of death (e.g., "sudden cardiac death"). The Medical Monitor was changed and the contact information was revised. Language was modified to clarify the reporting requirements of all protocol-defined adverse events of special interest. The Roche study number (GO01297) was added to the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported