Clinical trial results:
A Multicenter, Phase III, Open-Label, Randomized Study in Previously Untreated Patients With Advanced Indolent Non-Hodgkin's Lymphoma Evaluating the Benefit of GA101 (RO5072759) Plus Chemotherapy Compared with Rituximab Plus Chemotherapy Followed by GA101 or Rituximab Maintenance Therapy in Responders

Summary

EudraCT number	2010-024132-41
Trial protocol	BE GB CZ SE DE HU FR ES IT FI
Global end of trial date	30 July 2021

Results information

Result version number	v3 (current)
This version publication date	25 August 2022
First version publication date	16 March 2017
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	BO21223

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01332968
WHO universal trial number (UTN)	-
Other trial identifiers	Study name: GALLIUM

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 July 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 January 2016
Global end of trial reached?	Yes
Global end of trial date	30 July 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of obinutuzumab (RO5072759) in combination with chemotherapy compared to rituximab (MabThera/Rituxan) with chemotherapy followed by obinutuzumab or rituximab maintenance in subjects with previously untreated advanced follicular non-Hodgkin's lymphoma.

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	06 July 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	China: 58
Country: Number of subjects enrolled	Japan: 129
Country: Number of subjects enrolled	Taiwan: 4
Country: Number of subjects enrolled	Czechia: 100
Country: Number of subjects enrolled	Hungary: 71
Country: Number of subjects enrolled	Russian Federation: 12
Country: Number of subjects enrolled	Canada: 138
Country: Number of subjects enrolled	United States: 31
Country: Number of subjects enrolled	Australia: 135
Country: Number of subjects enrolled	Israel: 6
Country: Number of subjects enrolled	Belgium: 35
Country: Number of subjects enrolled	Germany: 237
Country: Number of subjects enrolled	Spain: 48
Country: Number of subjects enrolled	Finland: 4
Country: Number of subjects enrolled	France: 30
Country: Number of subjects enrolled	United Kingdom: 294
Country: Number of subjects enrolled	Italy: 59
Country: Number of subjects enrolled	Sweden: 10

Worldwide total number of subjects	1401
EEA total number of subjects	594

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)	937
From 65 to 84 years	454
85 years and over	10

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 177 centers in 18 countries.

Pre-assignment

Screening details:

Eleven patients withdrew from the study after randomization but prior to receiving study treatment.

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	Rituximab+Chemotherapy – Induction

Arm description:

Subjects received either 8 cycles of rituximab along with 6 cycles of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) (21-day cycle) or 8 cycles of rituximab along with 8 cycles of cyclophosphamide, vincristine, and prednisone (CVP) (21-day cycles) or 6 cycles of rituximab along with 6 cycles of bendamustine (28-day cycle) during induction period. The chemotherapy regimen (CHOP or CVP or bendamustine) for individual subject was chosen by the site prior to initiation of the study.

Arm type	Active comparator
Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cyclophosphamide 750 milligrams per square metre (mg/m^2) will be administered intravenously (IV) on Day 1 of each cycle during induction period.

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

Dosage and administration details:

Doxorubicin 50 mg/m^2 IV will be administered on Day 1 of each cycle during induction period.

Investigational medicinal product name	Vincristine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vincristine 1.4 mg/m^2 (maximum 2 mg) IV will be administered on Day 1 of each cycle during induction period.

Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Prednisone 100 mg (or equivalent prednisolone or methylprednisolone) will be administered orally on Days 1-5 of each cycle during induction period

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:

Bendamustine 90 mg/m^2 IV infusion will be administered on Days 1 and 2 of each cycle during induction period.

Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	MabThera/Rituxan
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Rituximab 375 mg/m^2 IV infusion will be administered on Day 1 of each cycle during induction period and rituximab 375 mg/m^2 every 2 months during maintenance period.

Arm title	Obinutuzumab+Chemotherapy – Induction

Arm description:

Subjects received either 8 cycles of obinutuzumab along with 6 cycles of CHOP (21-day cycle) or 8 cycles of obinutuzumab along with 8 cycles of CVP (21-day cycles) or 6 cycles of obinutuzumab along with 6 cycles of bendamustine (28-day cycle) during induction period. The chemotherapy regimen (CHOP or CVP or bendamustine) for individual subject was chosen by the site prior to initiation of the study.

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

Dosage and administration details:

Obinutuzumab 1000 mg IV infusion will be administered on Day 1, 8, and 15 of Cycle 1 and then on Day 1 of each subsequent cycle during induction period and obinutuzumab 1000 mg IV infusion every 2 months during maintenance period.

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

Dosage and administration details:

Cyclophosphamide 750 mg/m^2 IV will be administered on Day 1 of each cycle during induction period.

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

Dosage and administration details:

Doxorubicin 50 mg/m^2 IV will be administered on Day 1 of each cycle during induction period.

Investigational medicinal product name	Vincristine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion

Routes of administration	Intravenous use

Dosage and administration details:

Vincristine 1.4 mg/m^2 (maximum 2 mg) IV will be administered on Day 1 of each cycle during induction period.

Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Prednisone 100 mg (or equivalent prednisolone or methylprednisolone) will be administered orally on Days 1-5 of each cycle during induction period

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:

Bendamustine 90 mg/m^2 IV infusion will be administered on Days 1 and 2 of each cycle during induction period.

Arm title	Rituximab+Chemotherapy – Maintenance

Arm description:

The induction period was followed by either a maintenance or observation period for responders or non-responders, respectively. Responders received rituximab monotherapy every 2 months for 2 years during the maintenance period.

Arm type	Active comparator
Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	MabThera/Rituxan
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Rituximab 375 mg/m^2 IV infusion will be administered on Day 1 of each cycle during induction period and rituximab 375 mg/m^2 every 2 months during maintenance period.

Arm title	Obinutuzumab+Chemotherapy – Maintenance

Arm description:

The induction period was followed by either a maintenance or observation period for responders or non-responders, respectively. Responders received obinutuzumab monotherapy every 2 months for 2 years during the maintenance period.

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

Dosage and administration details:

Obinutuzumab 1000 mg IV infusion will be administered on Day 1, 8, and 15 of Cycle 1 and then on Day 1 of each subsequent cycle during induction period and obinutuzumab 1000 mg IV infusion every 2 months during maintenance period.

Arm title	Rituximab+Chemotherapy – Observation

Arm description:

The induction period was followed by either a maintenance or observation period for responders or non-responders, respectively. Non-responders received no protocol specified treatment during the 2-year observation period.

Arm type	Active comparator
Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	MabThera/Rituxan
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Rituximab 375 mg/m^2 IV infusion will be administered on Day 1 of each cycle during induction period and rituximab 375 mg/m^2 every 2 months during maintenance period.

Arm title	Obinutuzumab+Chemotherapy – Observation

Arm description:

The induction period was followed by either a maintenance or observation period for responders or non-responders, respectively. Non-responders received no protocol specified treatment during the 2-year observation period.

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

Dosage and administration details:

Obinutuzumab 1000 mg IV infusion will be administered on Day 1, 8, and 15 of Cycle 1 and then on Day 1 of each subsequent cycle during induction period and obinutuzumab 1000 mg IV infusion every 2 months during maintenance period.

Arm title	Rituximab+Chemotherapy – Follow-up

Arm description:

Finally, subjects were followed during a 5-year follow-up period.

Arm type	Active comparator
Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	MabThera/Rituxan
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Rituximab 375 mg/m^2 IV infusion will be administered on Day 1 of each cycle during induction period and rituximab 375 mg/m^2 every 2 months during maintenance period.

Arm title	Obinutuzumab+Chemotherapy – Follow-up

Arm description:

Finally, subjects were followed during a 5-year follow-up period.

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

Dosage and administration details:

Obinutuzumab 1000 mg IV infusion will be administered on Day 1, 8, and 15 of Cycle 1 and then on Day 1 of each subsequent cycle during induction period and obinutuzumab 1000 mg IV infusion every 2 months during maintenance period.

Number of subjects in period 1	Rituximab+Chemotherapy – Induction	Obinutuzumab+Chemotherapy – Induction	Rituximab+Chemotherapy – Maintenance
Started	699	702	612
Completed	641	646	451
Not completed	58	56	161
Physician decision	6	1	14
Adverse Event	23	26	53
Death	1	4	5
Progressive Disease	15	7	72
Not Specified	2	2	4
Non-compliance	1	-	4
Randomised but not treated	4	7	-
Withdrawal by Subject	3	5	7
Lost to follow-up	-	-	1
Protocol deviation	3	4	1
No reason provided	-	-	-

Number of subjects in period 1	Obinutuzumab+Chemotherapy – Maintenance	Rituximab+Chemotherapy – Observation	Obinutuzumab+Chemotherapy – Observation
Started	624	12	11
Completed	475	12	10
Not completed	149	0	1
Physician decision	19	-	1
Adverse Event	66	-	-
Death	6	-	-
Progressive Disease	40	-	-
Not Specified	7	-	-
Non-compliance	3	-	-
Randomised but not treated	-	-	-
Withdrawal by Subject	5	-	-
Lost to follow-up	2	-	-
Protocol deviation	1	-	-
No reason provided	-	-	-

Number of subjects in period 1	Rituximab+Chemotherapy – Follow-up	Obinutuzumab+Chemotherapy – Follow-up
Started	554	602
Completed	324	367
Not completed	230	235
Physician decision	12	15
Adverse Event	-	4

Death	27	30
Progressive Disease	126	106
Not Specified	18	21
Non-compliance	4	9
Randomised but not treated	-	-
Withdrawal by Subject	29	32
Lost to follow-up	11	15
Protocol deviation	1	-
No reason provided	2	3

Baseline characteristics

Reporting groups

Reporting group title	Overall Period

Reporting group description: -

Reporting group values	Overall Period	Total	
Number of subjects	1401	1401	
Age Categorical Units: Subjects			
Adults (18-64 years)	937	937	
From 65-84 years	454	454	
85 years and over	10	10	
Age Continuous Units: years			
arithmetic mean	58.5		
standard deviation	± 11.9	-	
Gender Categorical Units: Subjects			
Female	739	739	
Male	662	662	
Age Continuous in Follicular Lymphoma Sub-Population			
Age continuous for subjects with follicular lymphoma, who encompassed the population for the primary endpoint (n=601 for each arm in the follicular lymphoma intent-to-treat population).			
Units: years			
arithmetic mean	57.9		
standard deviation	± 11.9	-	

Subject analysis sets

Subject analysis set title	Rituximab+Chemotherapy
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Subjects received either 8 cycles of rituximab along with 6 cycles of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) (21-day cycle) or 8 cycles of rituximab along with 8 cycles of cyclophosphamide, vincristine, and prednisone (CVP) (21-day cycles) or 6 cycles of rituximab along with 6 cycles of bendamustine (28-day cycle) during the induction period. The induction period was followed by either a maintenance or observation period for responders or non-responders, respectively. Responders received rituximab monotherapy every 2 months for 2 years during the maintenance period. Non-responders received no protocol specified treatment during the 2-year observation period. Finally, subjects were followed during a 5-year follow-up period. The chemotherapy regimen (CHOP or CVP or bendamustine) for individual subject was chosen by the site prior to initiation of the study.

Subject analysis set title	Obinutuzumab+Chemotherapy
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Subjects received either 8 cycles of obinutuzumab along with 6 cycles of CHOP (21-day cycle) or 8 cycles of obinutuzumab along with 8 cycles of CVP (21-day cycles) or 6 cycles of obinutuzumab along with 6 cycles of bendamustine (28-day cycle) during induction period. The induction period was followed by either a maintenance or observation period for responders or non-responders, respectively. Responders received obinutuzumab monotherapy every 2 months for 2 years during the maintenance period. Non-responders received no protocol specified treatment during the 2-year observation period. Finally, subjects were followed during a 5-year follow-up period. The chemotherapy regimen (CHOP or

CVP or bendamustine) for individual subject was chosen by the site prior to initiation of the study.

Reporting group values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy	
Number of subjects	699	702	
Age Categorical Units: Subjects			
Adults (18-64 years)	473	464	
From 65-84 years	221	233	
85 years and over	5	5	
Age Continuous Units: years			
arithmetic mean	58.1	58.9	
standard deviation	± 12.3	± 11.6	
Gender Categorical Units: Subjects			
Female	374	365	
Male	325	337	
Age Continuous in Follicular Lymphoma Sub-Population			
Age continuous for subjects with follicular lymphoma, who encompassed the population for the primary endpoint (n=601 for each arm in the follicular lymphoma intent-to-treat population).			
Units: years			
arithmetic mean	57.7	58.2	
standard deviation	± 12.2	± 11.5	

End points reporting groups

Reporting group title	Rituximab+Chemotherapy – Induction

Reporting group description:

Subjects received either 8 cycles of rituximab along with 6 cycles of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) (21-day cycle) or 8 cycles of rituximab along with 8 cycles of cyclophosphamide, vincristine, and prednisone (CVP) (21-day cycles) or 6 cycles of rituximab along with 6 cycles of bendamustine (28-day cycle) during induction period. The chemotherapy regimen (CHOP or CVP or bendamustine) for individual subject was chosen by the site prior to initiation of the study.

Reporting group title	Obinutuzumab+Chemotherapy – Induction

Reporting group description:

Subjects received either 8 cycles of obinutuzumab along with 6 cycles of CHOP (21-day cycle) or 8 cycles of obinutuzumab along with 8 cycles of CVP (21-day cycles) or 6 cycles of obinutuzumab along with 6 cycles of bendamustine (28-day cycle) during induction period. The chemotherapy regimen (CHOP or CVP or bendamustine) for individual subject was chosen by the site prior to initiation of the study.

Reporting group title	Rituximab+Chemotherapy – Maintenance

Reporting group description:

The induction period was followed by either a maintenance or observation period for responders or non-responders, respectively. Responders received rituximab monotherapy every 2 months for 2 years during the maintenance period.

Reporting group title	Obinutuzumab+Chemotherapy – Maintenance

Reporting group description:

The induction period was followed by either a maintenance or observation period for responders or non-responders, respectively. Responders received obinutuzumab monotherapy every 2 months for 2 years during the maintenance period.

Reporting group title	Rituximab+Chemotherapy – Observation

Reporting group description:

The induction period was followed by either a maintenance or observation period for responders or non-responders, respectively. Non-responders received no protocol specified treatment during the 2-year observation period.

Reporting group title	Obinutuzumab+Chemotherapy – Observation

Reporting group description:

The induction period was followed by either a maintenance or observation period for responders or non-responders, respectively. Non-responders received no protocol specified treatment during the 2-year observation period.

Reporting group title	Rituximab+Chemotherapy – Follow-up

Reporting group description:

Finally, subjects were followed during a 5-year follow-up period.

Reporting group title	Obinutuzumab+Chemotherapy – Follow-up

Reporting group description:

Finally, subjects were followed during a 5-year follow-up period.

Subject analysis set title	Rituximab+Chemotherapy
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Subjects received either 8 cycles of rituximab along with 6 cycles of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) (21-day cycle) or 8 cycles of rituximab along with 8 cycles of cyclophosphamide, vincristine, and prednisone (CVP) (21-day cycles) or 6 cycles of rituximab along with 6 cycles of bendamustine (28-day cycle) during the induction period. The induction period was followed by either a maintenance or observation period for responders or non-responders, respectively. Responders received rituximab monotherapy every 2 months for 2 years during the maintenance period. Non-responders received no protocol specified treatment during the 2-year observation period. Finally, subjects were followed during a 5-year follow-up period. The chemotherapy regimen (CHOP or CVP or bendamustine) for individual subject was chosen by the site prior to initiation of the study.

Subject analysis set title	Obinutuzumab+Chemotherapy
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Subjects received either 8 cycles of obinutuzumab along with 6 cycles of CHOP (21-day cycle) or 8 cycles of obinutuzumab along with 8 cycles of CVP (21-day cycles) or 6 cycles of obinutuzumab along with 6 cycles of bendamustine (28-day cycle) during induction period. The induction period was followed by either a maintenance or observation period for responders or non-responders, respectively. Responders received obinutuzumab monotherapy every 2 months for 2 years during the maintenance period. Non-responders received no protocol specified treatment during the 2-year observation period. Finally, subjects were followed during a 5-year follow-up period. The chemotherapy regimen (CHOP or CVP or bendamustine) for individual subject was chosen by the site prior to initiation of the study.

Primary: Progression-Free Survival (PFS) in the Follicular Lymphoma Population, Investigator-Assessed

End point title	Progression-Free Survival (PFS) in the Follicular Lymphoma Population, Investigator-Assessed

End point description:

PFS in subjects with follicular lymphoma was defined as the time from randomisation until the first documented day of disease progression or death from any cause, whichever occurred first, on the basis of investigator assessments according to the Revised Response Criteria for Malignant Lymphoma. Progression was defined as at least 50% increase in nodal lesions or >/=50% increase in any node > 1 centimetre (cm) or >/= 50% increase in other target measurable lesions and/or appearance of any new bone marrow involvement and/or appearance of any new lesion > 1.5 cm or >/= 50% increase in any previously involved node with a diameter </= 1 cm such that it is now >1.5 cm. Tumour measurements were obtained by computed tomography (CT) or magnetic resonance imaging (MRI). FL ITT population was defined as all randomized participants with follicular histology, where participants were grouped according to their randomized treatment arm regardless of what treatments were actually received.

End point type	Primary

End point timeframe:

Baseline up to data cut-off (up to approximately 4 years and 7 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	601	601		
Units: percentage of subjects with event				
number (not applicable)	24.0	16.8		

Statistical analyses

Statistical analysis title	Rituximab versus Obinutuzumab
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0012 [1]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.66

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	0.85

Notes:

[1] - Stratified by chemotherapy regimen and Follicular Lymphoma International Prognostic Index (FLIPI) risk group.

Secondary: Progression-Free Survival in the Follicular Lymphoma Population, Investigator-Assessed

End point title	Progression-Free Survival in the Follicular Lymphoma Population, Investigator-Assessed

End point description:

PFS in subjects with follicular lymphoma was defined as the time from randomisation until the first documented day of disease progression or death from any cause, whichever occurred first, on the basis of investigator assessments according to the Revised Response Criteria for Malignant Lymphoma. Progression was defined as at least 50% increase in nodal lesions or >/=50% increase in any node > 1 centimetre (cm) or >/= 50% increase in other target measurable lesions and/or appearance of any new bone marrow involvement and/or appearance of any new lesion > 1.5 cm or >/= 50% increase in any previously involved node with a diameter </= 1 cm such that it is now >1.5 cm. Tumour measurements were obtained by computed tomography (CT) or magnetic resonance imaging (MRI). FL ITT population was defined as all randomized participants with follicular histology, where participants were grouped according to their randomized treatment arm regardless of what treatments were actually received.

End point type	Secondary

End point timeframe:

Baseline up to final analysis (up to 10 years)

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	601	601		
Units: percentage of subjects with event				
number (not applicable)	40.6	34.3		

Statistical analyses

Statistical analysis title	Rituximab versus Obinutuzumab
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0055
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.77

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	0.93

Secondary: Progression-Free Survival in the Overall Study Population, Investigator-Assessed

End point title	Progression-Free Survival in the Overall Study Population, Investigator-Assessed

End point description:

PFS in the overall study population was defined as the time from randomisation until the first documented day of disease progression or death from any cause, whichever occurred first, on the basis of investigator assessments according to the Revised Response Criteria for Malignant Lymphoma. Progression was defined as at least 50% increase in nodal lesions or >/=50% increase in any node > 1 centimeter (cm) or >/= 50% increase in other target measurable lesions (e.g., splenic or hepatic nodules) and/or appearance of any new bone marrow involvement and/or appearance of any new lesion > 1.5 cm or >/= 50% increase in any previously involved node with a diameter </= 1 cm such that it is now >1.5 cm. Tumour measurements were obtained by CT/MRI. The ITT population was defined as all randomised subjects grouped according to their randomised treatment arm regardless of what treatments were actually received.

End point type	Secondary

End point timeframe:

Baseline up to data cut-off (up to approximately 5 years and 2 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	699	702		
Units: percentage of subjects with event				
number (not applicable)	41.5	34.8		

Statistical analyses

Statistical analysis title	Rituximab versus Obinutuzumab
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1401
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0028
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.77

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	0.91

Secondary: Progression-Free Survival (PFS) (Follicular Lymphoma Population), IRC-Assessed

End point title	Progression-Free Survival (PFS) (Follicular Lymphoma Population), IRC-Assessed

End point description:

PFS in the subjects with follicular lymphoma was defined as the time from randomisation until the first documented day of disease progression or death from any cause, whichever occurred first, on the basis of IRC assessments according to the Revised Response Criteria for Malignant Lymphoma. Progression was defined as at least 50% increase in nodal lesions or >/=50% increase in any node > 1 centimeter (cm) or >/= 50% increase in other target measurable lesions (e.g., splenic or hepatic nodules) and/or appearance of any new bone marrow involvement and/or appearance of any new lesion > 1.5 cm or >/= 50% increase in any previously involved node with a diameter </= 1 cm such that it is now >1.5 cm. Tumour measurements were obtained by CT/MRI. The FL ITT population was defined as all randomised subjects with follicular histology grouped according to their randomised treatment arm regardless of what treatments were actually received.

End point type	Secondary

End point timeframe:

Baseline up to data cut-off (up to approximately 5 years and 2 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	601	601		
Units: percentage of subjects with event				
number (not applicable)	23.5	18.0		

Statistical analyses

Statistical analysis title	Rituximab versus Obinutuzumab
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0118
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.72

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	0.93

Secondary: Progression-Free Survival (PFS) (Overall Study Population), Assessed by Independent Review Committee (IRC)

End point title	Progression-Free Survival (PFS) (Overall Study Population), Assessed by Independent Review Committee (IRC)

End point description:

PFS in the overall study population was defined as the time from randomisation until the first documented day of disease progression or death from any cause, whichever occurred first, on the basis of IRC assessments according to the Revised Response Criteria for Malignant Lymphoma. Progression was defined as at least 50% increase in nodal lesions or >/=50% increase in any node > 1 centimeter (cm) or >/= 50% increase in other target measurable lesions (e.g., splenic or hepatic nodules) and/or appearance of any new bone marrow involvement and/or appearance of any new lesion > 1.5 cm or >/= 50% increase in any previously involved node with a diameter </= 1 cm such that it is now >1.5 cm. Tumour measurements were obtained by CT/MRI. The ITT population was defined as all randomised subjects grouped according to their randomised treatment arm regardless of what treatments were actually received.

End point type	Secondary

End point timeframe:

Baseline up to data cut-off (up to approximately 5 years and 2 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	699	702		
Units: percentage of subjects with event				
number (not applicable)	24.6	18.4		

Statistical analyses

Statistical analysis title	Rituximab versus Obinutuzumab
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1401
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0038
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.71

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	0.9

Secondary: Overall Response (Follicular Lymphoma Population), Investigator-Assessed

End point title	Overall Response (Follicular Lymphoma Population), Investigator-Assessed

End point description:

Percentage of subjects with overall response in the follicular lymphoma population was defined as percentage of subjects with PR or complete response CR determined on the basis of investigator assessments with the use of Revised Response Criteria for Malignant Lymphoma. Tumour assessments were performed with CT/MRI with or without PET. CR was defined as disappearance of all target lesions; PR was defined as >=50% decrease target lesions in up to six dominant lesions identified at baseline, no new lesions and no increase in the size of the liver, spleen, or other nodes. Splenic and hepatic nodules must have regressed by >/= 50%. Overall Response (OR) = CR + PR. The FL ITT population was defined as all randomised subjects with follicular histology grouped according to their randomised treatment arm regardless of what treatments were actually received.

End point type	Secondary

End point timeframe:

Baseline up to end of induction period (up to approximately 7 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	601	601		
Units: percentage of subjects with event				
number (not applicable)				
Without PET (n=519, 530)	86.4	88.2		
With PET (n=242, 254)	81.2	85.5		

Statistical analyses

Statistical analysis title	Without PET
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3
Method	Logrank
Parameter estimate	Absolute difference in %
Point estimate	1.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.02
upper limit	5.68

Statistical analysis title	With PET
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.17
Method	Logrank
Parameter estimate	Absolute difference in %
Point estimate	4.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	10.5

Secondary: Overall Response (Overall Study Population), Investigator-Assessed

End point title	Overall Response (Overall Study Population), Investigator-Assessed

End point description:

Percentage of subjects with overall response in the overall study population was defined as percentage of subjects with partial response (PR) or complete response (CR) determined on the basis of investigator assessments with the use of Revised Response Criteria for Malignant Lymphoma. Tumour assessments were performed with CT/MRI with or without positron emission tomography (PET). CR was defined as disappearance of all target lesions; PR was defined as >=50% decrease target lesions in up to six dominant lesions identified at baseline, no new lesions and no increase in the size of the liver, spleen, or other nodes. Splenic and hepatic nodules must have regressed by >/= 50%; Overall Response (OR) = CR + PR. The ITT population was defined as all randomised subjects grouped according to their randomised treatment arm regardless of what treatments were actually received.

End point type	Secondary

End point timeframe:

Baseline up to end of induction period (up to approximately 7 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	699	702		
Units: percentage of subjects with event				
number (not applicable)				
Without PET (n=599, 613)	85.7	87.3		
With PET (n=270, 274)	81.8	85.4		

Statistical analyses

Statistical analysis title	With PET
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1401
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.17
Method	Logrank
Parameter estimate	Absolute difference in %
Point estimate	3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	9.4

Statistical analysis title	Without PET
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1401
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.33
Method	Logrank
Parameter estimate	Absolute difference in %
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	5.3

Secondary: Complete Response (Follicular Lymphoma Population), Investigator-Assessed

End point title	Complete Response (Follicular Lymphoma Population), Investigator-Assessed

End point description:

Complete response in the follicular lymphoma population was determined on the basis of investigator assessments with the use of Revised Response Criteria for Malignant Lymphoma. Tumour assessments were performed with CT/MRI with or without PET. CR was defined as disappearance of all target lesions. The FL ITT population was defined as all randomised subjects with follicular histology grouped according to their randomised treatment arm regardless of what treatments were actually received.

End point type	Secondary

End point timeframe:

Baseline up to end of induction period (up to approximately 7 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	601	601		
Units: percentage of subjects with event				
number (not applicable)				
Without PET (n=145, 112)	24.1	18.6		
With PET (n=169, 184)	56.7	62.0		

Statistical analyses

Statistical analysis title	Without PET
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02
Method	Logrank
Parameter estimate	Absolute difference in %
Point estimate	-5.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.2
upper limit	-0.78

Statistical analysis title	With PET
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.32
Method	Logrank
Parameter estimate	Absolute difference in %
Point estimate	5.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	13.3

Secondary: Complete Response (Overall Study Population), Investigator-Assessed

End point title	Complete Response (Overall Study Population), Investigator-Assessed

End point description:

Complete response in the overall study population was determined on the basis of investigator assessments with the use of Revised Response Criteria for Malignant Lymphoma. Tumor assessments were performed with CT/MRI with or without PET. CR was defined as disappearance of all target lesions. The ITT population was defined as all randomised subjects grouped according to their randomised treatment arm regardless of what treatments were actually received. Reported is the percentage of subjects with event.

End point type	Secondary

End point timeframe:

Baseline up to end of induction period (up to approximately 7 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	699	702		
Units: percentage of subjects with event				
number (not applicable)				
Without PET (n=163, 129)	23.3	18.4		
With PET (n=188, 196)	57.0	61.1		

Statistical analyses

Statistical analysis title	With PET
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1401
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.33
Method	Logrank
Parameter estimate	Absolute difference in %
Point estimate	4.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	11.8

Statistical analysis title	Without PET
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1401
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02
Method	Logrank
Parameter estimate	Absolute difference in %
Point estimate	-4.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.3
upper limit	0.6

Secondary: Overall Response (Follicular Lymphoma Population), IRC-Assessed

End point title	Overall Response (Follicular Lymphoma Population), IRC-Assessed

End point description:

Percentage of subjects with overall response in the follicular lymphoma population was defined as percentage of subjects with PR or complete response CR determined on the basis of IRC assessments with the use of Revised Response Criteria for Malignant Lymphoma. Tumour assessments were performed with CT/MRI with or without PET. CR was defined as disappearance of all target lesions; PR was defined as >=50% decrease target lesions in up to six dominant lesions identified at baseline, no new lesions and no increase in the size of the liver, spleen, or other nodes. Splenic and hepatic nodules must have regressed by >/= 50%. Overall Response (OR) = CR + PR. The FL ITT population was defined as all randomised subjects with follicular histology grouped according to their randomised treatment arm regardless of what treatments were actually received.

End point type	Secondary

End point timeframe:

Baseline up to end of induction period (up to approximately 7 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	601	601		
Units: percentage of subjects with event				
number (not applicable)				
Without PET (n=529, 549)	88.0	91.3		
With PET (n=254, 263)	85.2	88.6		

Statistical analyses

Statistical analysis title	Without PET
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.052
Method	Logrank
Parameter estimate	Absolute difference in %
Point estimate	3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.19
upper limit	6.85

Statistical analysis title	With PET
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3
Method	Logrank
Parameter estimate	Absolute difference in %
Point estimate	3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	8.9

Secondary: Overall Response (Overall Study Population), IRC-Assessed

End point title	Overall Response (Overall Study Population), IRC-Assessed

End point description:

Percentage of subjects with overall response in the overall study population was defined as percentage of subjects with PR or CR determined on the basis of IRC assessments with the use of Revised Response Criteria for Malignant Lymphoma. Tumour assessments were performed with CT/MRI with or without PET. CR was defined as disappearance of all target lesions; PR was defined as >=50% decrease target lesions in up to six dominant lesions identified at baseline, no new lesions and no increase in the size of the liver, spleen, or other nodes. Splenic and hepatic nodules must have regressed by >/= 50%; Overall Response (OR) = CR + PR. The ITT population was defined as all randomised subjects grouped according to their randomised treatment arm regardless of what treatments were actually received.

End point type	Secondary

End point timeframe:

Baseline up to end of induction period (up to approximately 7 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	699	702		
Units: percentage of subjects with event				
number (not applicable)				
Without PET (n=606, 631)	86.7	89.9		
With PET (n=330, 321)	83.3	87.2		

Statistical analyses

Statistical analysis title	Without PET
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1401
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.049
Method	Logrank
Parameter estimate	Absolute difference in %
Point estimate	3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	6.6

Statistical analysis title	With PET
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1401
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.22
Method	Logrank
Parameter estimate	Absolute difference in %
Point estimate	3.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	9.5

Secondary: Complete Response (Follicular Lymphoma Population), IRC-Assessed	
End point title	Complete Response (Follicular Lymphoma Population), IRC-Assessed

End point description:

Complete response in the follicular lymphoma population was determined on the basis of IRC assessments with the use of Revised Response Criteria for Malignant Lymphoma. Tumour assessments were performed with CT/MRI with or without PET. CR was defined as disappearance of all target lesions. The FL ITT population was defined as all randomised subjects with follicular histology grouped according to their randomised treatment arm regardless of what treatments were actually received.

End point type	Secondary

End point timeframe:

Baseline up to end of induction period (up to approximately 7 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	601	601		
Units: percentage of subjects with event				
number (not applicable)				
Without PET (n=161, 171)	26.8	28.5		
With PET (n=178, 212)	59.7	71.4		

Statistical analyses

Statistical analysis title	Wirh PET
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Logrank
Parameter estimate	Absolute difference in %
Point estimate	11.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.9
upper limit	19.4

Statistical analysis title	Without PET
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.58
Method	Logrank
Parameter estimate	Absolute difference in %
Point estimate	1.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	6.8

Secondary: Complete Response (Overall Study Population), IRC-Assessed

End point title	Complete Response (Overall Study Population), IRC-Assessed

End point description:

Complete response in the overall study population was determined on the basis of IRC assessments with the use of Revised Response Criteria for Malignant Lymphoma. Tumour assessments were performed with CT/MRI with or without PET. CR was defined as disappearance of all target lesions. The ITT population was defined as all randomised subjects grouped according to their randomised treatment arm regardless of what treatments were actually received.

End point type	Secondary

End point timeframe:

Baseline up to end of induction period (up to approximately 7 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	699	702		
Units: percentage of subjects with event				
number (not applicable)				
Without PET (n=184, 190)	26.3	27.1		
With PET (n=196, 223)	59.4	69.5		

Statistical analyses

Statistical analysis title	Without PET
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1401
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8
Method	Logrank
Parameter estimate	Absolute difference in %
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	5.5

Statistical analysis title	With PET
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1401
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	Logrank
Parameter estimate	Absolute difference in %
Point estimate	10.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.6
upper limit	17.6

Secondary: Overall Survival (Follicular Lymphoma Population)

End point title	Overall Survival (Follicular Lymphoma Population)

End point description:

Overall survival in the follicular lymphoma population was defined as the time from the date of randomisation to the date of death from any cause. The FL ITT population was defined as all randomised subjects with follicular histology grouped according to their randomised treatment arm regardless of what treatments were actually received. Reported is the percentage of subjects with event.

End point type	Secondary

End point timeframe:

Baseline up to 10 years

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	601	601		
Units: percentage of subjects with event				
number (not applicable)	14.3	12.6		

Statistical analyses

Statistical analysis title	Rituximab versus Obinutuzumab
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy

Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3577
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.18

Secondary: Overall Survival (Overall Study Population)

End point title	Overall Survival (Overall Study Population)

End point description:

Overall survival in the overall study population was defined as the time from the date of randomisation to the date of death from any cause. The ITT population was defined as all randomised subjects grouped according to their randomised treatment arm regardless of what treatments were actually received. Reported is the percentage of subjects with event.

End point type	Secondary

End point timeframe:

Baseline up to data cut-off (up to approximately 5 years and 2 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	699	702		
Units: percentage of subjects with event				
number (not applicable)	10.2	8.4		

Statistical analyses

Statistical analysis title	Rituximab versus Obinutuzumab
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1401
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.25
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.82

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	1.16

Secondary: Event-Free Survival (Follicular Lymphoma Population)

End point title	Event-Free Survival (Follicular Lymphoma Population)

End point description:

Event-free survival: time from the date of randomisation to the date to disease progression/relapse, death from any cause, or initiation of a new anti-lymphoma treatment (NALT) on the basis of investigator assessment assessments with the use of Revised Response Criteria for Malignant Lymphoma. Disease progression/relapse was defined as at least 50% increase in nodal lesions or >/=50% increase in any node > 1 centimeter (cm) or >/= 50% increase in other target measurable lesions (e.g., splenic or hepatic nodules) and/or appearance of any new bone marrow involvement and/or appearance of any new lesion > 1.5 cm or >/= 50% increase in any previously involved node with a diameter </= 1 cm such that it is now >1.5 cm. Tumour measurements were obtained by CT/MRI. FL ITT population: all randomised subjects with follicular histology grouped according to their randomised treatment arm regardless of what treatments were actually received. Reported: percentage of subjects with event

End point type	Secondary

End point timeframe:

Baseline up to 10 years

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	601	601		
Units: percentage of subjects with event				
number (not applicable)	42.9	35.8		

Statistical analyses

Statistical analysis title	Rituximab versus Obinutuzumab
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0015
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.74

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	0.89

Secondary: Event-Free Survival (Overall Study Population)

End point title	Event-Free Survival (Overall Study Population)

End point description:

Event-free survival was defined as the time from the date of randomisation to the date to disease progression/relapse, death from any cause, or initiation of a new anti-lymphoma treatment (NALT) on the basis of investigator assessment assessments with the use of Revised Response Criteria for Malignant Lymphoma. Disease progression/relapse was defined as at least 50% increase in nodal lesions or >/=50% increase in any node > 1 centimeter (cm) or >/= 50% increase in other target measurable lesions (e.g., splenic or hepatic nodules) and/or appearance of any new bone marrow involvement and/or appearance of any new lesion > 1.5 cm or >/= 50% increase in any previously involved node with a diameter </= 1 cm such that it is now >1.5 cm. Tumour measurements were obtained by CT/MRI. The ITT population was defined as all randomised subjects grouped according to their randomised treatment arm regardless of what treatments were actually received. Reported: percentage of subjects with event.

End point type	Secondary

End point timeframe:

Baseline up to data cut-off (up to approximately 4 years and 7 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	699	702		
Units: percentage of subjects with event				
number (not applicable)	30.6	22.6		

Statistical analyses

Statistical analysis title	Rituximab versus Obinutuzumab
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1401
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0004
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.69

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	0.85

Secondary: Disease-Free Survival (DFS), (Follicular Lymphoma Population)

End point title	Disease-Free Survival (DFS), (Follicular Lymphoma Population)

End point description:

DFS: time from the date of the first occurrence of a documented CR to the date of disease progression/ relapse, or death from any cause on the basis of investigator assessments with the use of Revised Response Criteria for Malignant Lymphoma. Tumour assessments were performed with CT/MRI. CR was defined as disappearance of all target lesions. Progression/relapse was defined as at least 50% increase in nodal lesions or >/=50% increase in any node > 1 centimeter (cm) or >/= 50% increase in other target measurable lesions (e.g., splenic or hepatic nodules) and/or appearance of any new bone marrow involvement and/or appearance of any new lesion > 1.5 cm or >/= 50% increase in any previously involved node with a diameter </= 1 cm such that it is now >1.5 cm. Subjects with CR within the FL ITT population were included in the analysis. Reported: percentage of subjects with event.

End point type	Secondary

End point timeframe:

From first occurrence of documented CR to data cut-off (up to approximately 5 years and 2 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	330	355		
Units: percentage of subjects with event				
number (not applicable)	27.9	26.3		

Statistical analyses

Statistical analysis title	Rituximab versus Obinutuzumab
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	685
Analysis specification	Pre-specified
Analysis type	superiority
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.27

Secondary: Disease-Free Survival (DFS) (Overall Study Population)

End point title	Disease-Free Survival (DFS) (Overall Study Population)

End point description:

DFS: time from the date of the first occurrence of a documented CR to the date of disease progression/ relapse, or death from any cause on the basis of investigator assessments with the use of Revised Response Criteria for Malignant Lymphoma. Tumour assessments were performed with CT/MRI. CR was defined as disappearance of all target lesions. Progression/relapse was defined as at least 50% increase in nodal lesions or >/=50% increase in any node > 1 centimeter (cm) or >/= 50% increase in other target measurable lesions (e.g., splenic or hepatic nodules) and/or appearance of any new bone marrow involvement and/or appearance of any new lesion > 1.5 cm or >/= 50% increase in any previously involved node with a diameter </= 1 cm such that it is now >1.5 cm. Subjects with CR within the ITT population were included in the analysis. Reported: percentage of subjects with event.

End point type	Secondary

End point timeframe:

From first occurrence of documented CR to data cut-off (up to approximately 5 years and 2 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab +Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	320	343		
Units: percentage of subjects with event				
number (not applicable)	14.9	11.2		

Statistical analyses

Statistical analysis title	Rituximab versus Obinutuzumab
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	663
Analysis specification	Pre-specified
Analysis type	superiority
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.19

Secondary: Duration of Response (DOR) (Follicular Lymphoma Population), Investigator-Assessed

End point title	Duration of Response (DOR) (Follicular Lymphoma Population),

	Investigator-Assessed

End point description:

DOR was defined as the time from first occurrence of a documented CR or PR to disease progression/relapse, or death from any cause. Tumour assessments by CT/MRI. CR: disappearance of all target lesions. PR: >/=50% decrease target lesions in up to six dominant lesions identified at baseline, no new lesions, no increase in the size of the liver, spleen, or other nodes. Splenic and hepatic nodules must have regressed by >/= 50%. Progression/relapse was defined as at least 50% increase in nodal lesions or >/=50% increase in any node > 1 centimeter (cm) or >/= 50% increase in other target measurable lesions (e.g., splenic or hepatic nodules) and/or appearance of any new bone marrow involvement and/or appearance of any new lesion > 1.5 cm or >/= 50% increase in any previously involved node with a diameter </= 1 cm such that it is now >1.5 cm.Subjects with CR or PR within the FL ITT population were included in the analysis. Reported is the percentage of subjects with event.

End point type	Secondary

End point timeframe:

From first occurrence of documented CR or PR to data cut-off (up to approximately 5 years and 2 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	568	571		
Units: percentage of subjects with event				
number (not applicable)	39.3	33.3		

Statistical analyses

Statistical analysis title	Rituximab versus Obinutuzumab
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1139
Analysis specification	Pre-specified
Analysis type	superiority
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	0.93

Secondary: Duration of Response (DOR) (Overall Study Population), Investigator-Assessed

End point title	Duration of Response (DOR) (Overall Study Population), Investigator-Assessed

End point description:

DOR was defined as the time from first occurrence of a documented CR or PR to disease progression/relapse, or death from any cause. Tumour assessments by CT/MRI. CR: disappearance of all

target lesions. PR: >/=50% decrease target lesions in up to six dominant lesions identified at baseline, no new lesions and no increase in the size of the liver, spleen, or other nodes. Splenic and hepatic nodules must have regressed by >/= 50%. Progression/relapse was defined as at least 50% increase in nodal lesions or >/=50% increase in any node > 1 centimeter (cm) or >/= 50% increase in other target measurable lesions (e.g., splenic or hepatic nodules) and/or appearance of any new bone marrow involvement and/or appearance of any new lesion > 1.5 cm or >/= 50% increase in any previously involved node with a diameter </= 1 cm such that it is now >1.5 cm. Subjects with CR or PR within the ITT population were included in the analysis. Reported is the percentage of subjects with event.

End point type	Secondary

End point timeframe:

From first occurrence of documented CR or PR to data cut-off (up to approximately 5 years and 2 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	656	659		
Units: percentage of subjects with event				
number (not applicable)	25.5	18.7		

Statistical analyses

Statistical analysis title	Rituximab versus Obinutuzumab
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1315
Analysis specification	Pre-specified
Analysis type	superiority
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	0.88

Secondary: Time to Next Anti-Lymphoma Treatment (Follicular Lymphoma Population)

End point title	Time to Next Anti-Lymphoma Treatment (Follicular Lymphoma Population)

End point description:

Time to next anti-lymphoma treatment was defined as the time from the date of randomisation to the start date of the next anti-lymphoma treatment or death from any cause. Reported is the percentage of subjects who started next anti-lymphoma treatment. The FL ITT population was defined as all randomised subjects with follicular histology grouped according to their randomised treatment arm regardless of what treatments were actually received. Reported is the percentage of subjects with event.

End point type	Secondary

End point timeframe:

Baseline up to 10 years

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	601	601		
Units: percentage of subjects with event				
number (not applicable)	34.8	26.6		

Statistical analyses

Statistical analysis title	Rituximab versus Obinutuzumab
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	superiority
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	0.87

Secondary: Time to Next Anti-Lymphoma Treatment (Overall Study Population)

End point title	Time to Next Anti-Lymphoma Treatment (Overall Study Population)

End point description:

Time to next anti-lymphoma treatment was defined as the time from the date of randomisation to the start date of the next anti-lymphoma treatment or death from any cause. Reported is the percentage of subjects who started next anti-lymphoma treatment. The ITT population was defined as all randomised subjects grouped according to their randomised treatment arm regardless of what treatments were actually received. Reported is the percentage of subjects with event.

End point type	Secondary

End point timeframe:

Baseline up to data cut-off (up to approximately 5 years and 2 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	699	702		
Units: percentage of subjects with event				
number (not applicable)	21.6	15.7		

Statistical analyses

Statistical analysis title	Rituximab versus Obinutuzumab
Comparison groups	Rituximab+Chemotherapy v Obinutuzumab+Chemotherapy
Number of subjects included in analysis	1401
Analysis specification	Pre-specified
Analysis type	superiority
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	0.89

Secondary: Percentage of Subjects With Adverse Events

End point title	Percentage of Subjects With Adverse Events

End point description:

An adverse event is any untoward medical occurrence in a subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with the treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. Preexisting conditions which worsen during a study are also considered as adverse events. The safety analysis population included all subjects who received any amount of any study drug and subjects were analysed according to the treatment received.

End point type	Secondary

End point timeframe:

Baseline up to 10 years

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	692	698		
Units: percentage of subjects				
number (not applicable)	99.6	99.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in All Domains of FACT-G (Follicular Lymphoma Population)

End point title	Change from Baseline in All Domains of FACT-G (Follicular Lymphoma Population)

End point description:

FACT-G consists of the following 4 FACT-Lym sub-questionnaires: Physical Well-being (range: 0-28), Social/Family Well-being (range: 0-28), Emotional Well-being (range: 0-24) and Functional Well-being (range: 0-28). Higher scores indicate better outcomes. A positive change from baseline indicates improvement. The FL ITT population was defined as all randomised subjects with follicular histology grouped according to their randomised treatment arm regardless of what treatments were actually received.

End point type	Secondary

End point timeframe:

Baseline (Induction Cycle 1, Day 1), end of study (up to approximately 5 years and 2 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	601	601		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Physical Well-being (PW), Baseline (n=557, n=566)	23.36 (± 4.77)	23.14 (± 4.85)		
PW Change, Cycle 3, Day 1 (n=511,496)	-0.91 (± 4.54)	-0.21 (± 4.59)		
PW Change, End Induction (n=482, 480)	-0.06 (± 4.83)	0.56 (± 5.14)		
PW Change, Maint Month 2 (n=362, 398)	0.83 (± 4.76)	1.42 (± 5.09)		
PW Change, Maint Month 12 (n=362, 406)	1.14 (± 4.29)	1.34 (± 4.74)		
PW Change, End Maint (n=411, 437)	0.88 (± 4.54)	1.33 (± 5.00)		
Social/Family Well-being , Baseline (n=555, 563)	22.84 (± 4.92)	23.28 (± 4.77)		
S/FW Change, Cycle 3 Day 1 (n=506, 492)	-0.52 (± 4.03)	-0.67 (± 3.92)		
S/FW Change, End Induction (n=482, 475)	-0.46 (± 4.77)	-0.56 (± 5.00)		
S/FW Change, Maint Month 2 (n=359, 396)	-0.39 (± 4.72)	-0.67 (± 4.68)		
S/FW Change, Maint Month 12 (n=359, 403)	-0.61 (± 5.56)	-0.97 (± 5.34)		
S/FW Change, End Maint (n=410, 436)	-0.93 (± 5.67)	-0.71 (± 5.54)		

Emotional Well-being (EW), Baseline (n=556, 563)	17.64 (± 4.19)	17.87 (± 4.13)		
EW Change, Cycle 3 Day 1 (n=503, 490)	1.49 (± 3.40)	1.35 (± 3.35)		
EW Change, End Induction (n=478, 476)	1.16 (± 3.90)	1.14 (± 3.87)		
EW Change, Maint Month 2 (n=359, 396)	1.77 (± 3.88)	1.49 (± 4.16)		
EW Change, Maint Month 12 (n=360, 402)	1.45 (± 3.92)	1.46 (± 3.88)		
EW Change, End Maint (n=405, 435)	1.43 (± 3.98)	1.49 (± 3.99)		
Functional Well-being (FW), Baseline (n=556, 563)	18.66 (± 6.19)	18.76 (± 5.98)		
FW Change, Cycle 3 Day 1 (n=504, 488)	-0.30 (± 5.30)	-0.07 (± 5.24)		
FW Change, End Induction (n=480, 476)	0.44 (± 5.63)	0.93 (± 5.85)		
FW Change, Maint Month 2 (n=359, 396)	1.04 (± 5.31)	1.25 (± 6.02)		
FW Change, Maint Month 12 (n=360, 402)	1.84 (± 5.54)	1.65 (± 5.95)		
FW Change, End Maint (n=406, 436)	1.40 (± 6.12)	1.72 (± 6.16)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in FACT-Lym Total Outcome Index (TOI) Score (Follicular Lymphoma Population)

End point title	Change From Baseline in FACT-Lym Total Outcome Index (TOI) Score (Follicular Lymphoma Population)

End point description:

The FACT-Lym TOI Score for the follicular lymphoma population was derived from the following 3 individual FACT-Lym questionnaire subscale scores: Physical Well-being (range: 0-28), Functional Well-being (range: 0-28) and Lymphoma (range: 0-60). The FACT-Lym TOI Score is the sum of the 3 individual subscales (range 0-116). Higher scores indicate better outcomes. A positive change from baseline indicates an improvement. The FL ITT population was defined as all randomised subjects with follicular histology grouped according to their randomised treatment arm regardless of what treatments were actually received.

End point type	Secondary

End point timeframe:

Baseline (Induction Cycle 1, Day 1), end of study (up to approximately 5 years and 2 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	601	601		
Units: Units on a scale				
arithmetic mean (standard deviation)				
TOI Score, Baseline (n=559, 567)	86.61 (± 18.16)	86.94 (± 18.05)		

TOI Score Change, Cycle 3 Day 1 (n=514, 497)	0.46 (± 15.03)	2.18 (± 15.95)		
TOI Score Change, End Induction (n=485, 481)	2.91 (± 17.00)	4.57 (± 16.71)		
TOI Score Change, Maint Month 2 (n=363, 400)	6.22 (± 16.16)	7.17 (± 16.57)		
TOI Score Change, Maint Month 12 (n=362, 408)	7.61 (± 15.62)	7.20 (± 16.75)		
TOI Score Change, End Maint (n=412, 440)	6.23 (± 17.06)	7.44 (± 16.96)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in FACT-Lym Individual Subscale Lymphoma Score (Follicular Population)

End point title	Change From Baseline in FACT-Lym Individual Subscale Lymphoma Score (Follicular Population)

End point description:

The FACT-Lym Individual Subscale Lymphoma Score for the follicular lymphoma population was derived from the Lymphoma subscale questionnaire (range: 0-60). Higher scores indicate better outcomes. A positive change from baseline indicates an improvement. The FL ITT population was defined as all randomised subjects with follicular histology grouped according to their randomised treatment arm regardless of what treatments were actually received.

End point type	Secondary

End point timeframe:

Baseline (Induction Cycle 1, Day 1), end of study (up to approximately 5 years and 2 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab +Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	601	601		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Lymphoma, Baseline (n=556, 563)	45.01 (± 9.37)	45.54 (± 9.29)		
Lymphoma Change, Cycle 3 Day 1 (n=509, 491)	2.04 (± 7.18)	2.71 (± 7.46)		
Lymphoma Change, End Induction (n=477, 478)	2.99 (± 8.63)	3.01 (± 8.36)		
Lymphoma Change, Maint Month 2 (n=360, 395)	4.80 (± 8.29)	4.52 (± 8.32)		
Lymphoma Change, Maint Month 12 (n=360, 404)	4.93 (± 8.34)	4.27 (± 8.31)		
Lymphoma Change, End Maint (n=407, 438)	4.31 (± 8.81)	4.57 (± 8.54)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Functional Assessment of Cancer Therapy-Lymphoma (FACT-Lym) Total Score (Follicular Population)

End point title	Change From Baseline in Functional Assessment of Cancer Therapy-Lymphoma (FACT-Lym) Total Score (Follicular Population)

End point description:

The FACT-Lym Total Score for the follicular lymphoma population was derived from the following 5 individual FACT-Lym questionnaire subscale scores: Physical Well-being (range: 0-28), Social/Family Well-being (range: 0-28), Emotional Well-being (range: 0-24),Functional Well-being (range: 0-28) and Lymphoma (range: 0-60). The FACT-Lym Total Score is the sum of all 5 individual subscales (range 0-168). Higher scores indicate better outcomes. A positive change from baseline indicates an improvement. The FL ITT population was defined as all randomised subjects with follicular histology grouped according to their randomised treatment arm regardless of what treatments were actually received.

End point type	Secondary

End point timeframe:

Baseline (Induction Cycle 1, Day 1), end of study (up to approximately 5 years and 2 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	601	601		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Total Score, Baseline (n=552, 559)	127.40 (± 22.43)	128.42 (± 22.16)		
Total Score Change, Cycle 3 Day 1 (n=499, 484)	1.98 (± 17.01)	3.21 (± 17.12)		
Total Score Change, End Induction (n=471, 471)	4.18 (± 19.75)	5.10 (± 20.03)		
Total Score Change, Maint Month 2 (n=356, 392)	8.40 (± 19.16)	8.13 (± 19.80)		
Total Score Change, Maint Month 12 (n=358, 396)	8.87 (± 19.31)	7.90 (± 19.55)		
Total Score Change, End Maint (n=401, 433)	7.43 (± 19.88)	8.80 (± 20.57)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Euro-Quality of Life-5 Dimensions (EQ-5D) Questionnaire Summary Score (Follicular Lymphoma Population) During Induction Phase

End point title	Change From Baseline in Euro-Quality of Life-5 Dimensions (EQ-5D) Questionnaire Summary Score (Follicular Lymphoma Population) During Induction Phase

End point description:

The EQ-5D is a quality of life questionnaire with five questions, each with three categories (no problem,

moderate problem, severe problems) and a visual analogue scale (VAS) from 0 (worst possible health state) to 100 (best possible health state. Summary score ranges from 0 to 1. Higher scores indicate better outcomes. A positive change from baseline indicates an improvement. The FL ITT population was defined as all randomised subjects with follicular histology grouped according to their randomised treatment arm regardless of what treatments were actually received. 9999=NE=Not estimable based on 0 or 1 subject evaluated.

End point type	Secondary

End point timeframe:

Induction: Cycle 1 Day 1 (Baseline), Cycle 3 Day 1, End of Induction (up to 7 months) (1 Cycle=21 or 28 days); Maintenance: 2, 12, 25 months after Day 1 of last induction cycle (Cycle 6 or 8), Follow-up; up to data cut-off (up to 5 years and 2 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	601	601		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline Induction (n=558, 559)	0.80 (± 0.24)	0.81 (± 0.21)		
Change Baseline, Cycle 1 Day 1 (n=0, 0)	9999 (± 9999)	9999 (± 9999)		
Change Baseline, Cycle 3 Day 1 (n=505, 487)	0.03 (± 0.21)	0.03 (± 0.20)		
Change Baseline, Induction Completion (n=468, 466)	0.04 (± 0.23)	0.03 (± 0.22)		
Change Baseline, Maint/Obs Month 2 (n=348, 377)	0.05 (± 0.23)	0.06 (± 0.22)		
Change Baseline, Maint/Obs Month 12 (n=2, 1)	0.00 (± 0.00)	-0.20 (± 9999)		
Change Baseline, Maint/Obs Completion (n=0, 1)	9999 (± 9999)	-0.10 (± 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in EQ-5D Questionnaire Summary Score (Follicular Lymphoma Population) During Maintenance/Observation Phase

End point title	Change From Baseline in EQ-5D Questionnaire Summary Score (Follicular Lymphoma Population) During Maintenance/Observation Phase

End point description:

The EQ-5D is a quality of life questionnaire with five questions, each with three categories (no problem, moderate problem, severe problems) and a visual analogue scale (VAS) from 0 (worst possible health state) to 100 (best possible health state. Summary score ranges from 0 to 1. Higher scores indicate better outcomes. A positive change from baseline indicates an improvement. The FL ITT population was defined as all randomised subjects with follicular histology grouped according to their randomised treatment arm regardless of what treatments were actually received. 9999=NE=Not estimable based on 0 subjects evaluated.

End point type	Secondary

End point timeframe:

Induction: Cycle 1 Day 1 (Baseline), Cycle 3 Day 1, End of Induction (up to 7 months) (1 Cycle=21 or 28 days); Maintenance: 2, 12, 25 months after Day 1 of last induction cycle (Cycle 6 or 8), Follow-up;

up to data cut-off (up to 5 years and 2 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	601	601		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change Baseline, Maint/Obs Month 2 (n=11, 14)	0.04 (± 0.34)	0.04 (± 0.14)		
Change Baseline, Maint/Obs Month 12 (n=354, 395)	0.06 (± 0.24)	0.06 (± 0.21)		
Change Baseline, Maint/Obs Completion (n=402, 421)	0.03 (± 0.23)	0.05 (± 0.23)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in EQ-5D Questionnaire Summary Score (Follicular Lymphoma Population) During Follow Up Phase

End point title	Change From Baseline in EQ-5D Questionnaire Summary Score (Follicular Lymphoma Population) During Follow Up Phase

End point description:

The EQ-5D is a quality of life questionnaire with five questions, each with three categories (no problem, moderate problem, severe problems) and a visual analogue scale (VAS) from 0 (worst possible health state) to 100 (best possible health state. Summary score ranges from 0 to 1. Higher scores indicate better outcomes. A positive change from baseline indicates an improvement. The FL ITT population was defined as all randomised subjects with follicular histology grouped according to their randomised treatment arm regardless of what treatments were actually received.

End point type	Secondary

End point timeframe:

Induction: Cycle 1 Day 1 (Baseline), Cycle 3 Day 1, End of Induction (up to 7 months) (1 Cycle=21 or 28 days); Maintenance: 2, 12, 25 months after Day 1 of last induction cycle (Cycle 6 or 8), Follow-up; up to data cut-off (up to 5 years and 2 months)

End point values	Rituximab+Chemotherapy	Obinutuzumab+Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	601	601		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change Baseline, Follow-up Month 36 (n=238, 248)	0.05 (± 0.24)	0.06 (± 0.23)		
Change Baseline, Follow-up Month 48 (n=73, 80)	0.05 (± 0.20)	0.06 (± 0.23)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 10 years

Adverse event reporting additional description:

The safety analysis population included all subjects who received any amount of any study drug and subjects were analysed according to the treatment received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Obinutuzumab+Chemotherapy

Reporting group description:

Participants will receive either 8 cycles of obinutuzumab along with 6 cycles of CHOP (21-day cycle) or 8 cycles of obinutuzumab along with 8 cycles of CVP (21-day cycles) or 6 cycles of obinutuzumab along with 6 cycles of bendamustine (28-day cycle) during induction period. The induction period will be followed by either a maintenance or observation period for responders or non-responders, respectively. Responders will receive obinutuzumab monotherapy every 2 months for 2 years during the maintenance period. Non-responders will receive no protocol specified treatment during the 2-year observation period. Finally, participants will be followed during a 5-year follow-up period. The chemotherapy regimen (CHOP or CVP or bendamustine) for individual participant will be chosen by the site prior to initiation of the study.

Reporting group title	Rituximab+Chemotherapy

Reporting group description:

Participants will receive either 8 cycles of rituximab along with 6 cycles of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) (21-day cycle) or 8 cycles of rituximab along with 8 cycles of cyclophosphamide, vincristine, and prednisone (CVP) (21-day cycles) or 6 cycles of rituximab along with 6 cycles of bendamustine (28-day cycle) during the induction period. The induction period will be followed by either a maintenance or observation period for responders or non-responders, respectively. Responders will receive rituximab monotherapy every 2 months for 2 years during the maintenance period. Non-responders will receive no protocol specified treatment during the 2-year observation period. Finally, participants will be followed during a 5-year follow-up period. The chemotherapy regimen (CHOP or CVP or bendamustine) for individual participant will be chosen by the site prior to initiation of the study.

Serious adverse events	Obinutuzumab+Chemotherapy	Rituximab+Chemotherapy	
Total subjects affected by serious adverse events			
subjects affected / exposed	361 / 698 (51.72%)	309 / 692 (44.65%)	
number of deaths (all causes)	104	111	
number of deaths resulting from adverse events	14	6	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ADENOCARCINOMA OF COLON			
subjects affected / exposed	2 / 698 (0.29%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHOLANGIOCARCINOMA			

subjects affected / exposed	0 / 698 (0.00%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 2	
RENAL CANCER			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATIC CANCER			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
KERATOACANTHOMA			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SQUAMOUS CELL BREAST CARCINOMA			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ADENOCARCINOMA METASTATIC			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LENTIGO MALIGNA			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LARYNGEAL SQUAMOUS CELL CARCINOMA			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SQUAMOUS CELL CARCINOMA			

subjects affected / exposed	2 / 698 (0.29%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PITUITARY TUMOUR BENIGN			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRIC CANCER			
subjects affected / exposed	2 / 698 (0.29%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	1 / 2	0 / 1	
DUCTAL ADENOCARCINOMA OF PANCREAS			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTRADUCTAL PROLIFERATIVE BREAST LESION			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYELODYSPLASTIC SYNDROME			
subjects affected / exposed	4 / 698 (0.57%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PAPILLARY THYROID CANCER			
subjects affected / exposed	2 / 698 (0.29%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VULVOVAGINAL WARTS			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
TRANSITIONAL CELL CARCINOMA			

subjects affected / exposed	2 / 698 (0.29%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HODGKIN'S DISEASE NODULAR SCLEROSIS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BASAL CELL CARCINOMA			
subjects affected / exposed	6 / 698 (0.86%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	1 / 7	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
BENIGN LARYNGEAL NEOPLASM			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUROENDOCRINE CARCINOMA OF THE SKIN			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
ACUTE MYELOID LEUKAEMIA			
subjects affected / exposed	2 / 698 (0.29%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	2 / 4	1 / 1	
deaths causally related to treatment / all	1 / 2	1 / 1	
TUMOUR FLARE			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SCHWANNOMA			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INVASIVE DUCTAL BREAST CARCINOMA			

subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NON-SMALL CELL LUNG CANCER			
subjects affected / exposed	2 / 698 (0.29%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
COLORECTAL CANCER			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SQUAMOUS CELL CARCINOMA OF SKIN			
subjects affected / exposed	5 / 698 (0.72%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
BOWEN'S DISEASE			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HODGKIN'S DISEASE			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PROSTATE CANCER			
subjects affected / exposed	5 / 698 (0.72%)	4 / 692 (0.58%)	
occurrences causally related to treatment / all	1 / 5	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
OESOPHAGEAL CARCINOMA			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
BLADDER TRANSITIONAL CELL CARCINOMA METASTATIC			

subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUNG NEOPLASM MALIGNANT			
subjects affected / exposed	0 / 698 (0.00%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 3	
NON-HODGKIN'S LYMPHOMA			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
CANCER PAIN			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCREATIC CARCINOMA			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
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 / 698 (0.14%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
INTRAOCULAR MELANOMA			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ADENOCARCINOMA			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RECTAL ADENOCARCINOMA			

subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACUTE LYMPHOCYTIC LEUKAEMIA			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
TONGUE NEOPLASM MALIGNANT STAGE UNSPECIFIED			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRIC ADENOMA			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BREAST CANCER			
subjects affected / exposed	6 / 698 (0.86%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	2 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
THYROID ADENOMA			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COLON CANCER			
subjects affected / exposed	1 / 698 (0.14%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	0 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
HORMONE RECEPTOR POSITIVE BREAST CANCER			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACOUSTIC NEUROMA			

subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL NEOPLASM			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MENINGIOMA			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLADDER TRANSITIONAL CELL CARCINOMA			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUNG ADENOCARCINOMA			
subjects affected / exposed	2 / 698 (0.29%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 1	1 / 1	
HODGKIN'S DISEASE STAGE II			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NON-SMALL CELL LUNG CANCER STAGE IV			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
UTERINE CANCER			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL CELL CARCINOMA			

subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
EMBOLISM			
subjects affected / exposed	0 / 698 (0.00%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEEP VEIN THROMBOSIS			
subjects affected / exposed	1 / 698 (0.14%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERIPHERAL ARTERY ANEURYSM			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERIPHERAL ISCHAEMIA			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PELVIC VENOUS THROMBOSIS			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
AXILLARY VEIN THROMBOSIS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (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	7 / 698 (1.00%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	5 / 7	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERTENSIVE URGENCY			

subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CIRCULATORY COLLAPSE			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERTENSIVE CRISIS			
subjects affected / exposed	2 / 698 (0.29%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
ABORTION			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
CHILLS			
subjects affected / exposed	4 / 698 (0.57%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	4 / 4	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERTHERMIA			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHEST DISCOMFORT			
subjects affected / exposed	2 / 698 (0.29%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PYREXIA			
subjects affected / exposed	37 / 698 (5.30%)	23 / 692 (3.32%)	
occurrences causally related to treatment / all	23 / 43	11 / 24	
deaths causally related to treatment / all	0 / 0	0 / 0	

MUCOSAL INFLAMMATION			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MULTIPLE ORGAN DYSFUNCTION SYNDROME			
subjects affected / exposed	0 / 698 (0.00%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
DEATH			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 1	
HYPERPLASIA			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ILL-DEFINED DISORDER			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
INFUSION SITE EXTRAVASATION			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ADVERSE DRUG REACTION			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
STENT-GRAFT ENDOLEAK			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NON-CARDIAC CHEST PAIN			

subjects affected / exposed	2 / 698 (0.29%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PAIN			
subjects affected / exposed	0 / 698 (0.00%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHEST PAIN			
subjects affected / exposed	1 / 698 (0.14%)	4 / 692 (0.58%)	
occurrences causally related to treatment / all	0 / 1	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
SWELLING FACE			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CYST RUPTURE			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	3 / 698 (0.43%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	1 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
HYPOGAMMAGLOBULINAEMIA			

subjects affected / exposed	0 / 698 (0.00%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
CYTOKINE RELEASE SYNDROME			
subjects affected / exposed	2 / 698 (0.29%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANAPHYLACTIC SHOCK			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DRUG HYPERSENSITIVITY			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ALLERGY TO ARTHROPOD BITE			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANAPHYLACTIC REACTION			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERSENSITIVITY			
subjects affected / exposed	0 / 698 (0.00%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			

PROSTATITIS			
subjects affected / exposed	1 / 698 (0.14%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
OVARIAN MASS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
OVARIAN CYST			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VULVOVAGINAL PAIN			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VAGINAL ULCERATION			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
PLEURISY			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRONCHOSPASM			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSPNOEA			
subjects affected / exposed	10 / 698 (1.43%)	8 / 692 (1.16%)	
occurrences causally related to treatment / all	8 / 12	4 / 8	
deaths causally related to treatment / all	0 / 1	0 / 0	

ACUTE LUNG INJURY			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
ACUTE RESPIRATORY DISTRESS SYNDROME			
subjects affected / exposed	2 / 698 (0.29%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
LUNG DISORDER			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (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	2 / 698 (0.29%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY ARREST			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTERSTITIAL LUNG DISEASE			
subjects affected / exposed	2 / 698 (0.29%)	4 / 692 (0.58%)	
occurrences causally related to treatment / all	2 / 2	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
PHARYNGEAL PARAESTHESIA			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY ARTERIAL HYPERTENSION			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PLEURAL EFFUSION			

subjects affected / exposed	5 / 698 (0.72%)	5 / 692 (0.72%)	
occurrences causally related to treatment / all	1 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
EMPHYSEMA			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
EPISTAXIS			
subjects affected / exposed	1 / 698 (0.14%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUNG CONSOLIDATION			
subjects affected / exposed	0 / 698 (0.00%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA ASPIRATION			
subjects affected / exposed	2 / 698 (0.29%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
ASTHMA			
subjects affected / exposed	2 / 698 (0.29%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONITIS			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PARANASAL CYST			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COUGH			

subjects affected / exposed	0 / 698 (0.00%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY DISORDER			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY OEDEMA			
subjects affected / exposed	2 / 698 (0.29%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PHARYNGEAL INFLAMMATION			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMOPTYSIS			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY CONGESTION			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMOTHORAX			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY EMBOLISM			

subjects affected / exposed	8 / 698 (1.15%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	2 / 11	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	1 / 698 (0.14%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 1	
PLEURITIC PAIN			
subjects affected / exposed	1 / 698 (0.14%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY FAILURE			
subjects affected / exposed	3 / 698 (0.43%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Psychiatric disorders			
SUBSTANCE-INDUCED PSYCHOTIC DISORDER			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEPRESSION			
subjects affected / exposed	3 / 698 (0.43%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
CONFUSIONAL STATE			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DELIRIUM			

subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUICIDE ATTEMPT			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANXIETY			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ALCOHOL PROBLEM			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
EMOTIONAL DISORDER			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MENTAL STATUS CHANGES			
subjects affected / exposed	2 / 698 (0.29%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PSYCHOTIC DISORDER			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
DEVICE BREAKAGE			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			

INTERNATIONAL NORMALISED RATIO INCREASED			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATIC ENZYME INCREASED			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLOOD CREATININE INCREASED			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
EASTERN COOPERATIVE ONCOLOGY GROUP PERFORMANCE STATUS WORSENED			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
WHITE BLOOD CELLS URINE POSITIVE			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIROVIRUS TEST POSITIVE			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ALANINE AMINOTRANSFERASE INCREASED			

subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
MENISCUS INJURY			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARTILAGE INJURY			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRAIN CONTUSION			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMOTHORAX TRAUMATIC			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUMBAR VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
THORACIC VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HUMERUS FRACTURE			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FALL			

subjects affected / exposed	3 / 698 (0.43%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MULTIPLE FRACTURES			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANASTOMOTIC STENOSIS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COMPRESSION FRACTURE			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LIGAMENT SPRAIN			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFUSION RELATED REACTION			
subjects affected / exposed	36 / 698 (5.16%)	19 / 692 (2.75%)	
occurrences causally related to treatment / all	42 / 42	21 / 21	
deaths causally related to treatment / all	0 / 0	0 / 0	
FOOT FRACTURE			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACCIDENT			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEMUR FRACTURE			

subjects affected / exposed	2 / 698 (0.29%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
UPPER LIMB FRACTURE			
subjects affected / exposed	1 / 698 (0.14%)	4 / 692 (0.58%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
FACIAL BONES FRACTURE			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
POST PROCEDURAL HAEMORRHAGE			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MEDICATION ERROR			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SPINAL COMPRESSION FRACTURE			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANKLE FRACTURE			
subjects affected / exposed	1 / 698 (0.14%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAND FRACTURE			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ALCOHOL POISONING			

subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (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	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
HEREDITARY MOTOR AND SENSORY NEUROPATHY			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
CARDIOGENIC SHOCK			
subjects affected / exposed	2 / 698 (0.29%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
SINUS TACHYCARDIA			
subjects affected / exposed	3 / 698 (0.43%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TACHYCARDIA			
subjects affected / exposed	3 / 698 (0.43%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CORONARY ARTERY DISEASE			
subjects affected / exposed	1 / 698 (0.14%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRADYCARDIA			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

ARRHYTHMIA			
subjects affected / exposed	2 / 698 (0.29%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VENTRICULAR TACHYCARDIA			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PALPITATIONS			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
AORTIC VALVE STENOSIS			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYOCARDIAL ISCHAEMIA			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RIGHT VENTRICULAR FAILURE			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIAL FLUTTER			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACUTE MYOCARDIAL INFARCTION			

subjects affected / exposed	4 / 698 (0.57%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIO-RESPIRATORY ARREST			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CORONARY ARTERY STENOSIS			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC ARREST			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
ATRIAL FIBRILLATION			
subjects affected / exposed	9 / 698 (1.29%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	1 / 11	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC FAILURE CONGESTIVE			
subjects affected / exposed	2 / 698 (0.29%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYOCARDIAL INFARCTION			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
SINUS BRADYCARDIA			
subjects affected / exposed	5 / 698 (0.72%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	5 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC FAILURE			

subjects affected / exposed	2 / 698 (0.29%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	2 / 3	3 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
ANGINA PECTORIS			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
HAEMORRHAGIC STROKE			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CEREBRAL ISCHAEMIA			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LOSS OF CONSCIOUSNESS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEMENTIA			
subjects affected / exposed	2 / 698 (0.29%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LETHARGY			
subjects affected / exposed	2 / 698 (0.29%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	5 / 698 (0.72%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	1 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSDIADOCHOKINESIS			

subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIZZINESS POSTURAL			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUBARACHNOID HAEMORRHAGE			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CEREBRAL DISORDER			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PRESYNCOPE			
subjects affected / exposed	0 / 698 (0.00%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
MONOPARESIS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CEREBRAL INFARCTION			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
EPILEPSY			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FACIAL PARALYSIS			

subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ISCHAEMIC STROKE			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
HAEMORRHAGE INTRACRANIAL			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SPINAL CORD COMPRESSION			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEURALGIA			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SYNCOPE			
subjects affected / exposed	4 / 698 (0.57%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	1 / 4	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
POLYNEUROPATHY			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
BRACHIAL PLEXOPATHY			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIZZINESS			

subjects affected / exposed	1 / 698 (0.14%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATAXIA			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CAROTID ARTERY STENOSIS			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENCEPHALOPATHY			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
TREMOR			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ORTHOSTATIC INTOLERANCE			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERAMMONAEMIC ENCEPHALOPATHY			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
AMYOTROPHIC LATERAL SCLEROSIS			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
PARKINSON'S DISEASE			

subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ORTHOSTATIC TREMOR			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOTONIA			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEIZURE			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	0 / 698 (0.00%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
CEREBRAL HAEMATOMA			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
NERVOUS SYSTEM DISORDER			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUROPATHY PERIPHERAL			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
HAEMOLYSIS			

subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
AUTOIMMUNE HAEMOLYTIC ANAEMIA			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
HAEMOLYTIC ANAEMIA			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYELOSUPPRESSION			
subjects affected / exposed	3 / 698 (0.43%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPENIA			
subjects affected / exposed	28 / 698 (4.01%)	33 / 692 (4.77%)	
occurrences causally related to treatment / all	30 / 31	43 / 46	
deaths causally related to treatment / all	0 / 0	0 / 0	
IMMUNE THROMBOCYTOPENIA			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANAEMIA			
subjects affected / exposed	6 / 698 (0.86%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	6 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DISSEMINATED INTRAVASCULAR COAGULATION			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEBRILE NEUTROPENIA			

subjects affected / exposed	36 / 698 (5.16%)	23 / 692 (3.32%)	
occurrences causally related to treatment / all	45 / 48	28 / 31	
deaths causally related to treatment / all	0 / 0	0 / 0	
GRANULOCYTOPENIA			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
THROMBOCYTOPENIA			
subjects affected / exposed	5 / 698 (0.72%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	12 / 12	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
SPLENOMEGALY			
subjects affected / exposed	2 / 698 (0.29%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEUKOPENIA			
subjects affected / exposed	4 / 698 (0.57%)	6 / 692 (0.87%)	
occurrences causally related to treatment / all	2 / 4	8 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
VERTIGO			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
EAR PAIN			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEAFNESS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			

CORNEAL OPACITY			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
MELAENA			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VOMITING			
subjects affected / exposed	5 / 698 (0.72%)	9 / 692 (1.30%)	
occurrences causally related to treatment / all	4 / 5	10 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
CONSTIPATION			
subjects affected / exposed	3 / 698 (0.43%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ASCITES			
subjects affected / exposed	1 / 698 (0.14%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCREATITIS ACUTE			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRITIS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTESTINAL OBSTRUCTION			
subjects affected / exposed	4 / 698 (0.57%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ILEUS			

subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTESTINAL ISCHAEMIA			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RECTAL HAEMORRHAGE			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MOUTH ULCERATION			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMORRHOIDS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTESTINAL POLYP			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SWOLLEN TONGUE			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRITIS EROSIVE			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
UPPER GASTROINTESTINAL HAEMORRHAGE			

subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
GASTRIC HAEMORRHAGE			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
COLITIS			
subjects affected / exposed	3 / 698 (0.43%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	1 / 3	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCREATITIS			
subjects affected / exposed	4 / 698 (0.57%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	1 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA			
subjects affected / exposed	11 / 698 (1.58%)	7 / 692 (1.01%)	
occurrences causally related to treatment / all	7 / 12	3 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENTEROVESICAL FISTULA			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HIATUS HERNIA			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
FAECALOMA			

subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
OBSTRUCTIVE PANCREATITIS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROENTERITIS EOSINOPHILIC			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTESTINAL VILLI ATROPHY			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMATEMESIS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MIKULICZ'S SYNDROME			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
LARGE INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRIC ULCER			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
UMBILICAL HERNIA			

subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 698 (0.00%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUBACUTE PANCREATITIS			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LARGE INTESTINE POLYP			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INGUINAL HERNIA			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CROHN'S DISEASE			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	2 / 698 (0.29%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NAUSEA			
subjects affected / exposed	5 / 698 (0.72%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	5 / 5	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABDOMINAL PAIN			

subjects affected / exposed	10 / 698 (1.43%)	6 / 692 (0.87%)	
occurrences causally related to treatment / all	1 / 11	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSPEPSIA			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
HEPATIC FUNCTION ABNORMAL			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DRUG-INDUCED LIVER INJURY			
subjects affected / exposed	2 / 698 (0.29%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BILE DUCT STONE			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHOLECYSTITIS ACUTE			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATITIS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BILE DUCT STENOSIS			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHOLANGITIS			

subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHOLELITHIASIS			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATITIS ACUTE			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATIC CIRRHOSIS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHOLECYSTITIS			
subjects affected / exposed	5 / 698 (0.72%)	6 / 692 (0.87%)	
occurrences causally related to treatment / all	0 / 6	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
BILIARY COLIC			
subjects affected / exposed	3 / 698 (0.43%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
RASH			
subjects affected / exposed	5 / 698 (0.72%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	3 / 5	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
DERMATITIS EXFOLIATIVE GENERALISED			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DRUG ERUPTION			

subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RASH MACULO-PAPULAR			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACTINIC KERATOSIS			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DERMATITIS CONTACT			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
URTICARIA			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
NEPHROLITHIASIS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL PELVIS FISTULA			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACUTE KIDNEY INJURY			
subjects affected / exposed	4 / 698 (0.57%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL PAIN			

subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL INFARCT			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL COLIC			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL FAILURE			
subjects affected / exposed	1 / 698 (0.14%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
URETERIC OBSTRUCTION			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
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			
FLANK PAIN			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PATHOLOGICAL FRACTURE			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TEMPOROMANDIBULAR JOINT SYNDROME			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ARTHROPATHY			

subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NECK PAIN			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYOPATHY			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ROTATOR CUFF SYNDROME			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYOSITIS			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SPINAL PAIN			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SYNOVITIS			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MUSCULAR WEAKNESS			

subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
OSTEITIS DEFORMANS			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SPINAL STENOSIS			
subjects affected / exposed	0 / 698 (0.00%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
BACK PAIN			
subjects affected / exposed	2 / 698 (0.29%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMARTHROSIS			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
OSTEOARTHRITIS			
subjects affected / exposed	2 / 698 (0.29%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
SERONEGATIVE ARTHRITIS			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
GASTROENTERITIS VIRAL			

subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENTEROCOCCAL INFECTION			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRONCHITIS			
subjects affected / exposed	9 / 698 (1.29%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	2 / 9	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
POST PROCEDURAL INFECTION			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPENIC SEPSIS			
subjects affected / exposed	6 / 698 (0.86%)	5 / 692 (0.72%)	
occurrences causally related to treatment / all	8 / 9	7 / 8	
deaths causally related to treatment / all	1 / 1	0 / 1	
INFLUENZA			
subjects affected / exposed	4 / 698 (0.57%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BREAST ABSCESS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MUCOSAL INFECTION			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
OOPHORITIS			

subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHRONIC SINUSITIS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CLOSTRIDIUM DIFFICILE COLITIS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RHINITIS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ORAL HERPES			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BACTERAEMIA			
subjects affected / exposed	1 / 698 (0.14%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTED CYST			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PYELONEPHRITIS			
subjects affected / exposed	2 / 698 (0.29%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERITONSILLAR ABSCESS			

subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COMPLICATED APPENDICITIS			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HERPES ZOSTER OTICUS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTION			
subjects affected / exposed	6 / 698 (0.86%)	10 / 692 (1.45%)	
occurrences causally related to treatment / all	2 / 7	3 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY SEPSIS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIVERTICULITIS			
subjects affected / exposed	1 / 698 (0.14%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PARAPHARYNGEAL SPACE INFECTION			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT INFECTION			
subjects affected / exposed	8 / 698 (1.15%)	7 / 692 (1.01%)	
occurrences causally related to treatment / all	2 / 8	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUROBORRELIOSIS			

subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTERVERTEBRAL DISCITIS			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SINUSITIS			
subjects affected / exposed	1 / 698 (0.14%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
SCROTAL ABSCESS			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CATHETER SITE CELLULITIS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DISSEMINATED VARICELLA ZOSTER VIRUS INFECTION			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SINUSITIS FUNGAL			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
EPIGLOTTITIS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HERPES ZOSTER			

subjects affected / exposed	9 / 698 (1.29%)	9 / 692 (1.30%)	
occurrences causally related to treatment / all	6 / 9	5 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
ESCHERICHIA URINARY TRACT INFECTION			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
OTITIS MEDIA CHRONIC			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MASTOIDITIS			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPSIS			
subjects affected / exposed	14 / 698 (2.01%)	9 / 692 (1.30%)	
occurrences causally related to treatment / all	8 / 18	5 / 9	
deaths causally related to treatment / all	0 / 2	0 / 1	
STAPHYLOCOCCAL BACTERAEMIA			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
CYSTITIS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CELLULITIS			
subjects affected / exposed	4 / 698 (0.57%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	1 / 4	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
CYTOMEGALOVIRUS INFECTION			

subjects affected / exposed	2 / 698 (0.29%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPTIC SHOCK			
subjects affected / exposed	0 / 698 (0.00%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Q FEVER			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CAMPYLOBACTER INFECTION			
subjects affected / exposed	2 / 698 (0.29%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VARICELLA ZOSTER SEPSIS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIRAL INFECTION			
subjects affected / exposed	1 / 698 (0.14%)	4 / 692 (0.58%)	
occurrences causally related to treatment / all	0 / 1	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABDOMINAL SEPSIS			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
ENCEPHALITIS ENTEROVIRAL			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ESCHERICHIA INFECTION			

subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SINUSITIS BACTERIAL			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATYPICAL PNEUMONIA			
subjects affected / exposed	1 / 698 (0.14%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	0 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPENIC INFECTION			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
TUBERCULOSIS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABSCESS INTESTINAL			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROENTERITIS			
subjects affected / exposed	7 / 698 (1.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	1 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMOCYSTIS JIROVECII PNEUMONIA			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TUBO-OVARIAN ABSCESS			

subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABSCESS			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEBRILE INFECTION			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUBCUTANEOUS ABSCESS			
subjects affected / exposed	0 / 698 (0.00%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERIODONTITIS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
APPENDICITIS			
subjects affected / exposed	1 / 698 (0.14%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEVICE RELATED SEPSIS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BK VIRUS INFECTION			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RHINOVIRUS INFECTION			

subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VASCULAR DEVICE INFECTION			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
OESOPHAGEAL CANDIDIASIS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIRAL MYOSITIS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	13 / 698 (1.86%)	9 / 692 (1.30%)	
occurrences causally related to treatment / all	8 / 23	2 / 9	
deaths causally related to treatment / all	1 / 2	0 / 0	
OESOPHAGEAL INFECTION			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ARTHRITIS BACTERIAL			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA BACTERIAL			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
UROSEPSIS			

subjects affected / exposed	4 / 698 (0.57%)	5 / 692 (0.72%)	
occurrences causally related to treatment / all	4 / 5	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	5 / 698 (0.72%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	2 / 7	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA FUNGAL			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
OVARIAN BACTERIAL INFECTION			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA			
subjects affected / exposed	51 / 698 (7.31%)	43 / 692 (6.21%)	
occurrences causally related to treatment / all	24 / 61	24 / 51	
deaths causally related to treatment / all	2 / 7	0 / 2	
SOFT TISSUE INFECTION			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ARTHRITIS INFECTIVE			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BACTERIAL TRACHEITIS			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEVICE RELATED INFECTION			

subjects affected / exposed	1 / 698 (0.14%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROENTERITIS ESCHERICHIA COLI			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA PNEUMOCOCCAL			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
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	6 / 698 (0.86%)	5 / 692 (0.72%)	
occurrences causally related to treatment / all	3 / 7	9 / 11	
deaths causally related to treatment / all	0 / 1	0 / 0	
MENINGITIS ENTEROVIRAL			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTIVE EXACERBATION OF CHRONIC OBSTRUCTIVE AIRWAYS DISEASE			
subjects affected / exposed	3 / 698 (0.43%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HERPES ZOSTER INFECTION NEUROLOGICAL			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

ENDOCARDITIS			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PELVIC ABSCESS			
subjects affected / exposed	2 / 698 (0.29%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMOCYSTIS JIROVECII INFECTION			
subjects affected / exposed	0 / 698 (0.00%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
HYPONATRAEMIA			
subjects affected / exposed	4 / 698 (0.57%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERCALCAEMIA			
subjects affected / exposed	2 / 698 (0.29%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
HYPERGLYCAEMIA			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEHYDRATION			
subjects affected / exposed	4 / 698 (0.57%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	2 / 4	1 / 2	
deaths causally related to treatment / all	1 / 1	0 / 0	
HYPOKALAEMIA			
subjects affected / exposed	1 / 698 (0.14%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

FLUID OVERLOAD			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TUMOUR LYSIS SYNDROME			
subjects affected / exposed	3 / 698 (0.43%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	3 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIABETES MELLITUS			
subjects affected / exposed	2 / 698 (0.29%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Obinutuzumab+Chemotherapy	Rituximab+Chemotherapy	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	690 / 698 (98.85%)	675 / 692 (97.54%)	
Vascular disorders			
FLUSHING			
subjects affected / exposed	46 / 698 (6.59%)	40 / 692 (5.78%)	
occurrences (all)	56	44	
HOT FLUSH			
subjects affected / exposed	38 / 698 (5.44%)	25 / 692 (3.61%)	
occurrences (all)	43	28	
HYPOTENSION			
subjects affected / exposed	44 / 698 (6.30%)	28 / 692 (4.05%)	
occurrences (all)	48	32	
HYPERTENSION			
subjects affected / exposed	64 / 698 (9.17%)	50 / 692 (7.23%)	
occurrences (all)	100	70	
General disorders and administration site conditions			
PAIN			
subjects affected / exposed	26 / 698 (3.72%)	35 / 692 (5.06%)	
occurrences (all)	28	40	

PYREXIA			
subjects affected / exposed	200 / 698 (28.65%)	150 / 692 (21.68%)	
occurrences (all)	277	231	
CHILLS			
subjects affected / exposed	126 / 698 (18.05%)	74 / 692 (10.69%)	
occurrences (all)	172	99	
CHEST DISCOMFORT			
subjects affected / exposed	43 / 698 (6.16%)	36 / 692 (5.20%)	
occurrences (all)	45	43	
FATIGUE			
subjects affected / exposed	275 / 698 (39.40%)	277 / 692 (40.03%)	
occurrences (all)	390	392	
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	34 / 698 (4.87%)	35 / 692 (5.06%)	
occurrences (all)	38	36	
ASTHENIA			
subjects affected / exposed	47 / 698 (6.73%)	44 / 692 (6.36%)	
occurrences (all)	56	55	
MUCOSAL INFLAMMATION			
subjects affected / exposed	36 / 698 (5.16%)	44 / 692 (6.36%)	
occurrences (all)	41	55	
OEDEMA PERIPHERAL			
subjects affected / exposed	46 / 698 (6.59%)	40 / 692 (5.78%)	
occurrences (all)	50	47	
Respiratory, thoracic and mediastinal disorders			
PRODUCTIVE COUGH			
subjects affected / exposed	42 / 698 (6.02%)	35 / 692 (5.06%)	
occurrences (all)	53	41	
OROPHARYNGEAL PAIN			
subjects affected / exposed	82 / 698 (11.75%)	73 / 692 (10.55%)	
occurrences (all)	98	87	
DYSPNOEA			
subjects affected / exposed	112 / 698 (16.05%)	88 / 692 (12.72%)	
occurrences (all)	131	101	
THROAT IRRITATION			

subjects affected / exposed	27 / 698 (3.87%)	37 / 692 (5.35%)	
occurrences (all)	27	40	
COUGH			
subjects affected / exposed	221 / 698 (31.66%)	185 / 692 (26.73%)	
occurrences (all)	305	248	
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	113 / 698 (16.19%)	89 / 692 (12.86%)	
occurrences (all)	131	98	
ANXIETY			
subjects affected / exposed	44 / 698 (6.30%)	29 / 692 (4.19%)	
occurrences (all)	47	31	
Investigations			
WEIGHT DECREASED			
subjects affected / exposed	35 / 698 (5.01%)	45 / 692 (6.50%)	
occurrences (all)	37	49	
Injury, poisoning and procedural complications			
INFUSION RELATED REACTION			
subjects affected / exposed	416 / 698 (59.60%)	347 / 692 (50.14%)	
occurrences (all)	699	569	
Nervous system disorders			
DYSGEUSIA			
subjects affected / exposed	38 / 698 (5.44%)	40 / 692 (5.78%)	
occurrences (all)	42	44	
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	59 / 698 (8.45%)	47 / 692 (6.79%)	
occurrences (all)	68	50	
HEADACHE			
subjects affected / exposed	155 / 698 (22.21%)	123 / 692 (17.77%)	
occurrences (all)	229	185	
DIZZINESS			
subjects affected / exposed	75 / 698 (10.74%)	57 / 692 (8.24%)	
occurrences (all)	88	69	
PARAESTHESIA			
subjects affected / exposed	62 / 698 (8.88%)	51 / 692 (7.37%)	
occurrences (all)	71	68	

NEUROPATHY PERIPHERAL			
subjects affected / exposed	51 / 698 (7.31%)	49 / 692 (7.08%)	
occurrences (all)	62	52	
Blood and lymphatic system disorders			
NEUTROPENIA			
subjects affected / exposed	348 / 698 (49.86%)	307 / 692 (44.36%)	
occurrences (all)	885	777	
ANAEMIA			
subjects affected / exposed	75 / 698 (10.74%)	72 / 692 (10.40%)	
occurrences (all)	88	95	
THROMBOCYTOPENIA			
subjects affected / exposed	90 / 698 (12.89%)	52 / 692 (7.51%)	
occurrences (all)	150	79	
LEUKOPENIA			
subjects affected / exposed	87 / 698 (12.46%)	91 / 692 (13.15%)	
occurrences (all)	222	267	
Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed	207 / 698 (29.66%)	168 / 692 (24.28%)	
occurrences (all)	318	253	
VOMITING			
subjects affected / exposed	182 / 698 (26.07%)	151 / 692 (21.82%)	
occurrences (all)	242	211	
CONSTIPATION			
subjects affected / exposed	249 / 698 (35.67%)	221 / 692 (31.94%)	
occurrences (all)	326	301	
DRY MOUTH			
subjects affected / exposed	36 / 698 (5.16%)	23 / 692 (3.32%)	
occurrences (all)	40	25	
ABDOMINAL PAIN			
subjects affected / exposed	69 / 698 (9.89%)	78 / 692 (11.27%)	
occurrences (all)	84	95	
STOMATITIS			
subjects affected / exposed	54 / 698 (7.74%)	55 / 692 (7.95%)	
occurrences (all)	72	71	
NAUSEA			

subjects affected / exposed	354 / 698 (50.72%)	338 / 692 (48.84%)	
occurrences (all)	594	577	
ABDOMINAL PAIN UPPER			
subjects affected / exposed	57 / 698 (8.17%)	53 / 692 (7.66%)	
occurrences (all)	64	60	
DYSPEPSIA			
subjects affected / exposed	65 / 698 (9.31%)	50 / 692 (7.23%)	
occurrences (all)	82	56	
Skin and subcutaneous tissue disorders			
RASH			
subjects affected / exposed	127 / 698 (18.19%)	131 / 692 (18.93%)	
occurrences (all)	162	170	
PRURITUS			
subjects affected / exposed	102 / 698 (14.61%)	94 / 692 (13.58%)	
occurrences (all)	124	116	
DRY SKIN			
subjects affected / exposed	40 / 698 (5.73%)	36 / 692 (5.20%)	
occurrences (all)	44	39	
ERYTHEMA			
subjects affected / exposed	37 / 698 (5.30%)	37 / 692 (5.35%)	
occurrences (all)	40	43	
NIGHT SWEATS			
subjects affected / exposed	32 / 698 (4.58%)	38 / 692 (5.49%)	
occurrences (all)	35	46	
ALOPECIA			
subjects affected / exposed	90 / 698 (12.89%)	77 / 692 (11.13%)	
occurrences (all)	94	78	
Musculoskeletal and connective tissue disorders			
MUSCLE SPASMS			
subjects affected / exposed	40 / 698 (5.73%)	42 / 692 (6.07%)	
occurrences (all)	46	49	
BACK PAIN			
subjects affected / exposed	99 / 698 (14.18%)	115 / 692 (16.62%)	
occurrences (all)	127	143	
BONE PAIN			

subjects affected / exposed	40 / 698 (5.73%)	44 / 692 (6.36%)	
occurrences (all)	46	56	
ARTHRALGIA			
subjects affected / exposed	144 / 698 (20.63%)	127 / 692 (18.35%)	
occurrences (all)	180	160	
MYALGIA			
subjects affected / exposed	53 / 698 (7.59%)	38 / 692 (5.49%)	
occurrences (all)	63	43	
PAIN IN EXTREMITY			
subjects affected / exposed	66 / 698 (9.46%)	65 / 692 (9.39%)	
occurrences (all)	75	79	
Infections and infestations			
RHINITIS			
subjects affected / exposed	59 / 698 (8.45%)	36 / 692 (5.20%)	
occurrences (all)	71	49	
SINUSITIS			
subjects affected / exposed	68 / 698 (9.74%)	47 / 692 (6.79%)	
occurrences (all)	92	58	
ORAL HERPES			
subjects affected / exposed	46 / 698 (6.59%)	43 / 692 (6.21%)	
occurrences (all)	54	48	
BRONCHITIS			
subjects affected / exposed	47 / 698 (6.73%)	42 / 692 (6.07%)	
occurrences (all)	69	53	
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	59 / 698 (8.45%)	71 / 692 (10.26%)	
occurrences (all)	97	105	
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	39 / 698 (5.59%)	35 / 692 (5.06%)	
occurrences (all)	67	43	
CONJUNCTIVITIS			
subjects affected / exposed	35 / 698 (5.01%)	26 / 692 (3.76%)	
occurrences (all)	42	30	
NASOPHARYNGITIS			

subjects affected / exposed	135 / 698 (19.34%)	143 / 692 (20.66%)	
occurrences (all)	200	224	
HERPES ZOSTER			
subjects affected / exposed	70 / 698 (10.03%)	40 / 692 (5.78%)	
occurrences (all)	75	46	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	153 / 698 (21.92%)	132 / 692 (19.08%)	
occurrences (all)	217	189	
PNEUMONIA			
subjects affected / exposed	47 / 698 (6.73%)	46 / 692 (6.65%)	
occurrences (all)	63	59	
URINARY TRACT INFECTION			
subjects affected / exposed	75 / 698 (10.74%)	66 / 692 (9.54%)	
occurrences (all)	111	100	
Metabolism and nutrition disorders			
HYPOKALAEMIA			
subjects affected / exposed	48 / 698 (6.88%)	29 / 692 (4.19%)	
occurrences (all)	72	43	
DECREASED APPETITE			
subjects affected / exposed	98 / 698 (14.04%)	91 / 692 (13.15%)	
occurrences (all)	114	103	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 July 2011	Allow for an early futility analysis of the first 170 randomized patients with follicular lymphoma based on the end-of-induction treatment complete response rates. The statistical methods sections were updated accordingly. Positron emission tomography (PET) was also made mandatory at screening and at end of induction therapy for the first 170 subjects with follicular lymphoma at all sites where PET scanners were available. The determination of minimal residual disease (MRD) based on polymerase chain reaction detection of BCL2/IgH-rearrangements within the malignant clone for all subjects with follicular lymphoma was also implemented.
16 July 2012	Implementation of a deoxyribonucleic acid (DNA) substudy in those subjects who give consent to the Roche Clinical Repository (RCR) and to DNA collection.
28 May 2013	Clarification of measuring and assessing the spleen and splenic response for marginal zone lymphoma (MZL) subjects.
22 March 2014	The Sponsor issued a Dear Investigator Letter (DIL) on 3 February 2014 to inform investigators about a higher incidence of thrombocytopenia and hemorrhagic events during the first cycle in participants with chronic lymphocytic leukemia (CLL) treated with obinutuzumab plus chlorambucil (GClb) as compared with participants treated with rituximab plus chlorambucil (RClb) or chlorambucil alone. Updates to guidelines regarding management of participants with thrombocytopenia. Evaluation of medical resource utilization was removed from the secondary objectives. The name of the study drug was updated from GA101 to obinutuzumab.
09 June 2017	The protocol was amended to consider second malignancies as an adverse event of special interest (AESI). The Medical Monitor for the study changed. Biomarker sample storage changed from 15 to 5 years after the completion of the study.
15 February 2020	The protocol was amended to collect response after progression and administration of new anti-lymphoma treatment (NALT). The Medical Monitor changed. Reference safety information was added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported