



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	

Results information

Result version number	v1
This version publication date	16 March 2017
First version publication date	16 March 2017

Trial information

Trial identification

Sponsor protocol code	BO21223
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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	Interim
Date of interim/final analysis	31 January 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 January 2016
Global end of trial reached?	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	Czech Republic: 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: 136
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: 293
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	887

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: -

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/m²) 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/m² 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/m² (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/m² IV infusion will be administered on Days 1 and 2 of each cycle during induction period.

Arm title	Rituximab+Chemotherapy – Maintenance
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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/m² IV infusion will be administered on Day 1 of each cycle during induction period and rituximab 375 mg/m² every 2 months during maintenance period.

Arm title	Obinutuzumab+Chemotherapy – Maintenance
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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
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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/m² IV infusion will be administered on Day 1 of each cycle during induction period and rituximab 375 mg/m² every 2 months during maintenance period.

Arm title	Obinutuzumab+Chemotherapy – Observation
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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
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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/m² IV infusion will be administered on Day 1 of each cycle during induction period and rituximab 375 mg/m² every 2 months during maintenance period.

Arm title	Obinutuzumab+Chemotherapy – Follow-up
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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	399
Not completed	58	56	213
Physician decision	6	1	14
Adverse Event	23	26	50
Death	1	4	5
Progressive Disease	15	7	72
Other Reason	2	2	4
Ongoing	-	-	54
Non-compliance	1	-	2
Randomised but not treated	4	7	-
Withdrawal by Subject	3	5	10
Lost to follow-up	-	-	1
Protocol deviation	3	4	1

Number of subjects in period 1	Obinutuzumab+Chemotherapy – Maintenance	Rituximab+Chemotherapy – Observation	Obinutuzumab+Chemotherapy – Observation
Started	624	12	11
Completed	417	2	2
Not completed	207	10	9
Physician decision	19	-	-
Adverse Event	65	-	-
Death	6	-	-
Progressive Disease	39	-	-
Other Reason	5	-	-
Ongoing	62	10	8
Non-compliance	3	-	1
Randomised but not treated	-	-	-
Withdrawal by Subject	5	-	-
Lost to follow-up	2	-	-
Protocol deviation	1	-	-

Number of subjects in period 1	Rituximab+Chemotherapy – Follow-up	Obinutuzumab+Chemotherapy – Follow-up
Started	542	531
Completed	0	0
Not completed	542	531
Physician decision	-	-
Adverse Event	-	-

Death	38	22
Progressive Disease	-	-
Other Reason	-	-
Ongoing	502	505
Non-compliance	-	-
Randomised but not treated	-	-
Withdrawal by Subject	1	2
Lost to follow-up	1	2
Protocol deviation	-	-

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

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

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
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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 $\geq 50\%$ increase in any node > 1 centimetre (cm) or $\geq 50\%$ 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 $\geq 50\%$ 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). The intent-to-treat follicular lymphoma population (FL ITT) was defined as all randomised subjects with follicular histology grouped according to treatment arm regardless of what treatments were actually received.

End point type	Primary
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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	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 Overall Study Population, Investigator-Assessed

End point title	Progression-Free Survival in the Overall Study Population, Investigator-Assessed
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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 $\geq 50\%$ increase in any node > 1 centimeter (cm) or $\geq 50\%$ 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 $\geq 50\%$ 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
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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)	24.5	17.4		

Statistical analyses

No statistical analyses for this end point

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)
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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 $\geq 50\%$ increase in any node > 1 centimeter (cm) or $\geq 50\%$ 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 $\geq 50\%$ 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
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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)	21.6	16.1		

Statistical analyses

No statistical analyses for this end point

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

End point title	Progression-Free Survival (PFS) (Follicular Lymphoma Population), IRC-Assessed
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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 $\geq 50\%$ increase in any node > 1 centimeter (cm) or $\geq 50\%$ 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 $\geq 50\%$ 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
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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)	20.8	15.5		

Statistical analyses

No statistical analyses for this end point

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

End point title	Overall Response (Overall Study Population), Investigator-Assessed
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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 $\geq 50\%$ 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 $\geq 50\%$; 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
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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	86.1	87.6		
With PET	82.1	85.7		

Statistical analyses

No statistical analyses for this end point

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

End point title	Overall Response (Follicular Lymphoma Population), Investigator-Assessed
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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 $\geq 50\%$ 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 $\geq 50\%$. 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
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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	86.9	88.5		
With PET	81.5	85.9		

Statistical analyses

No statistical analyses for this end point

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

End point title	Complete Response (Overall Study Population), Investigator-Assessed
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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
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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	23.2	18.9		
With PET	57.3	61.4		

Statistical analyses

No statistical analyses for this end point

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

Assessed

End point title	Complete Response (Follicular Lymphoma Population), Investigator-Assessed
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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
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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	23.8	19.5		
With PET	56.7	62.3		

Statistical analyses

No statistical analyses for this end point

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

End point title	Overall Response (Overall Study Population), IRC-Assessed
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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 $\geq 50\%$ 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 $\geq 50\%$; 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
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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	86.7	89.7		
With PET	83.3	87.2		

Statistical analyses

No statistical analyses for this end point

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

End point title	Overall Response (Follicular Lymphoma Population), IRC-Assessed
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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 $\geq 50\%$ 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 $\geq 50\%$. 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
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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	88	91.2		
With PET	85.2	88.6		

Statistical analyses

No statistical analyses for this end point

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

End point title	Complete Response (Overall Study Population), IRC-Assessed
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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
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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	25.9	26.9		
With PET	59.4	69.5		

Statistical analyses

No statistical analyses for this end point

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

End point title	Complete Response (Follicular Lymphoma Population), IRC-Assessed
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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
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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	26.5	28.5		
With PET	59.7	71.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (Overall Study Population)

End point title	Overall Survival (Overall Study Population)
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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
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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)	9	7.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (Follicular Lymphoma Population)

End point title	Overall Survival (Follicular Lymphoma Population)
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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
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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)	7.7	5.8		

Statistical analyses

No statistical analyses for this end point

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 $\geq 50\%$ increase in any node > 1 centimeter (cm) or $\geq 50\%$ 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 $\geq 50\%$ 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)	27	19.7		

Statistical analyses

No statistical analyses for this end point

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 $\geq 50\%$ increase in any node > 1 centimeter (cm) or $\geq 50\%$ 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 $\geq 50\%$ 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 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)	26.5	18.6		

Statistical analyses

No statistical analyses for this end point

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 $\geq 50\%$ increase in any node > 1 centimeter (cm) or $\geq 50\%$ 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 $\geq 50\%$ 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 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	320	343		
Units: percentage of subjects with event				
number (not applicable)	12.8	8.7		

Statistical analyses

No statistical analyses for this end point

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

End point title	Disease-Free Survival (DFS), (Follicular Lymphoma Population)
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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 $\geq 50\%$ increase in any node > 1 centimeter (cm) or $\geq 50\%$ 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 $\geq 50\%$ 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
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End point timeframe:

From first occurrence of documented CR 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	281	298		
Units: percentage of subjects with event				
number (not applicable)	11.7	9.1		

Statistical analyses

No statistical analyses for this end point

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

End point title	Duration of Response (DOR) (Overall Study Population), Investigator-Assessed
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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: $\geq 50\%$ 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 $\geq 50\%$. Progression/relapse was defined as at least 50% increase in nodal lesions or $\geq 50\%$ increase in any node > 1 centimeter (cm) or $\geq 50\%$ 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 $\geq 50\%$ 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 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	656	659		
Units: percentage of subjects with event				
number (not applicable)	22.1	15.6		

Statistical analyses

No statistical analyses for this end point

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

End point title	Duration of Response (DOR) (Follicular Lymphoma Population), Investigator-Assessed
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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: $\geq 50\%$ 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 $\geq 50\%$. Progression/relapse was defined as at least 50% increase in nodal lesions or $\geq 50\%$ increase in any node > 1 centimeter (cm) or $\geq 50\%$ 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 $\geq 50\%$ 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 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	567	571		
Units: percentage of subjects with event				
number (not applicable)	21.9	15.4		

Statistical analyses

No statistical analyses for this end point

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

End point title	Time to Next Anti-Lymphoma Treatment (Overall Study Population)
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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
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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)	19.7	14.7		

Statistical analyses

No statistical analyses for this end point

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

End point title	Time to Next Anti-Lymphoma Treatment (Follicular Lymphoma Population)
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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
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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)	18.5	13.3		

Statistical analyses

No statistical analyses for this end point

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 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	692	698		
Units: percentage of subjects				
number (not applicable)	98.6	99.6		

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)
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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
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End point timeframe:

Baseline (Induction Cycle 1, Day 1), end of study (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: Unitless score				
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=352, 370)	0.86 (± 4.61)	1.27 (± 5.01)		
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)		
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=352, 369)	-0.98 (± 5.64)	-0.64 (± 5.18)		
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 (± 3.4)	1.35 (± 3.35)		
EW Change, End Induction (n=478, 476)	1.16 (± 3.9)	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=347, 368)	1.37 (± 3.94)	1.49 (± 4.01)		
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)	-0.3 (± 5.3)	-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=348, 369)	1.37 (± 6.18)	1.79 (± 6.24)		

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)
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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
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End point timeframe:

Baseline (Induction Cycle 1, Day 1), end of study (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: Unitless score				
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)	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)	7.2 (± 16.75)		
TOI Score Change, End Maint (n=353, 373)	6.52 (± 17.01)	7.57 (± 17.28)		

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 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: Unitless score				
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)	4.8 (± 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=350, 371)	4.45 (± 8.83)	4.72 (± 8.73)		

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 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: Unitless score				
arithmetic mean (standard deviation)				
Total Score, Baseline (n=552, 559)	127.4 (± 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)	5.1 (± 20.03)		
Total Score Change, Maint Month 2 (n=356, 392)	8.4 (± 19.16)	8.13 (± 19.8)		
Total Score Change, Maint Month 12 (n=358, 396)	8.87 (± 19.31)	7.9 (± 19.55)		
Total Score Change, End Maint (n=344, 366)	7.48 (± 19.63)	8.83 (± 20.84)		

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
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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 fromto..... 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
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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 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: Unitless score				
arithmetic mean (standard deviation)				
Baseline Induction (n=558, 559)	0.8 (± 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 (± 0.2)		
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 (± 0)	-0.2 (± 9999)		
Change Baseline, Maint/Obs Completion (n=0, 1)	9999 (± 9999)	-0.1 (± 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
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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 fromto..... 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
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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 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: Unitless score				
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 (\pm 0.24)	0.06 (\pm 0.21)		
Change Baseline, Maint/Obs Completion (n=344, 355)	0.04 (\pm 0.24)	0.05 (\pm 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
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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 fromto..... 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
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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 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: Unitless score				
arithmetic mean (standard deviation)				
Change Baseline, Follow-up Month 36 (n=149, 151)	0.04 (\pm 0.23)	0.05 (\pm 0.25)		
Change Baseline, Follow-up Month 48 (n=26, 29)	0.07 (\pm 0.27)	0.08 (\pm 0.26)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

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

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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.1
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Reporting groups

Reporting group title	Obinutuzumab+Chemotherapy
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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 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 during induction was chosen by the site prior to initiation of the study.

Reporting group title	Rituximab+Chemotherapy
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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 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 during induction phase was 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	340 / 698 (48.71%)	286 / 692 (41.33%)	
number of deaths (all causes)	50	63	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
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	
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	
Acute myeloid leukaemia			
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	1 / 1	0 / 0	
Adenocarcinoma			
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 of colon			
subjects affected / exposed	1 / 698 (0.14%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenoma 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	
Basal cell carcinoma			
subjects affected / exposed	5 / 698 (0.72%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 6	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign neoplasm			
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	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	
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	
Colon cancer			
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 / 1	
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	
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 / 1	
Gastric 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 / 1	
Hepatic neoplasm			
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	
Hodgkin's disease			
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	
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	
Intraductal proliferative breast lesion			

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	
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	
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	
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	
Lung adenocarcinoma			
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	
Lung neoplasm malignant			
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	
Malignant melanoma			
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 / 1	
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	
Myelodysplastic 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	1 / 1	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	
Non-small cell lung 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 / 1	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	
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	
Oestrogen 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	
Papillary thyroid 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	
Prostate cancer			
subjects affected / exposed	3 / 698 (0.43%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 1	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	
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	
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	
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	
Squamous cell carcinoma			
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	
Squamous cell carcinoma of skin			
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	
Thyroid 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	
Transitional cell carcinoma			
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	
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	
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	
Vascular disorders			
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	
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	
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	
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	
Hypertensive crisis			
subjects affected / exposed	2 / 698 (0.29%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	2 / 3	0 / 1	
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	
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	
Surgical and medical procedures			
Cancer surgery			
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	
Ileectomy			
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	
Thyroidectomy			
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	
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			
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	
Chest discomfort			

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	2 / 698 (0.29%)	4 / 692 (0.58%)	
occurrences causally related to treatment / all	0 / 2	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
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	
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	
Death			
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	1 / 1	0 / 2	
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	
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	
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	
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	
Influenza like illness			
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	
Injection 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	
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	
Multi-organ failure			
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	
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	
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	
Pain			
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	
Pyrexia			

subjects affected / exposed	37 / 698 (5.30%)	24 / 692 (3.47%)	
occurrences causally related to treatment / all	23 / 42	12 / 25	
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	
Immune system disorders			
Allergy to anthropod 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	
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	
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	
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	
Hypogammaglobulinaemia			
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	
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			
Ovarian 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	
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	
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	
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	
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	
Respiratory, thoracic and mediastinal disorders			
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	

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	
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	
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	
Chronic obstructive pulmonary disease			
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 / 1	0 / 1	
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			
subjects affected / exposed	10 / 698 (1.43%)	8 / 692 (1.16%)	
occurrences causally related to treatment / all	7 / 12	3 / 8	
deaths causally related to treatment / all	0 / 1	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	
Emphysema			
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	
Epistaxis			

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	
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	
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	
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	
Lung consolidation			
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	
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	
Oropharyngeal pain			
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	
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	
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	
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	
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	
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	
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	
Pneumonia aspiration			
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	
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	
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	
Productive cough			

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 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	
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	
Pulmonary embolism			
subjects affected / exposed	8 / 698 (1.15%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	2 / 9	0 / 2	
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	
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	
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	
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	
Vocal cord thickening			

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	
Psychiatric disorders			
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	
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	
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	
Depression			
subjects affected / exposed	2 / 698 (0.29%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
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	
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	
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	
Investigations			
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	
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	
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	
Liver function test abnormal			
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	
Injury, poisoning and procedural complications			
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	
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	
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	
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	
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	
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	
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	
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	
Fall			

subjects affected / exposed	3 / 698 (0.43%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	1 / 5	0 / 1	
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	
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	
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	
Infusion related reaction			
subjects affected / exposed	36 / 698 (5.16%)	18 / 692 (2.60%)	
occurrences causally related to treatment / all	42 / 42	20 / 20	
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	
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	
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	
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	
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	
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	
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	
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	
Spinal 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	
Upper limb fracture			
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	
Congenital, familial and genetic disorders			
Peroneal muscular 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	
Cardiac disorders			

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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
Cardiac-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	
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	
Coronary artery disease			
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
Nervous system disorders			
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	
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	
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	
Cerebellar syndrome			
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	
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	
Cerebral 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	
Cerebrovascular accident			
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	
Dementia			
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	
Dizziness			

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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
Syncope			
subjects affected / exposed	3 / 698 (0.43%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	1 / 3	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
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	
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	
VIIth nerve 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	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 698 (0.72%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	6 / 6	0 / 0	
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	
Bone marrow failure			
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	
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	34 / 698 (4.87%)	24 / 692 (3.47%)	
occurrences causally related to treatment / all	42 / 45	29 / 32	
deaths causally related to treatment / all	0 / 0	0 / 0	
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	
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	
Histiocytosis haematophagic			
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	
Immune thrombocytopenic purpura			
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	
Leukopenia			
subjects affected / exposed	3 / 698 (0.43%)	5 / 692 (0.72%)	
occurrences causally related to treatment / all	2 / 3	5 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	25 / 698 (3.58%)	30 / 692 (4.34%)	
occurrences causally related to treatment / all	28 / 29	38 / 41	
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	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	5 / 698 (0.72%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	12 / 12	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Deaffness			
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	
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	
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			
Abdominal pain			
subjects affected / exposed	10 / 698 (1.43%)	5 / 692 (0.72%)	
occurrences causally related to treatment / all	1 / 11	1 / 5	
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	
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	
Colitis			
subjects affected / exposed	3 / 698 (0.43%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	0 / 3	1 / 2	
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	
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	
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	
Dysphagia			
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
Inguinal hernia			
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 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	
Intestinal obstruction			

subjects affected / exposed	3 / 698 (0.43%)	0 / 692 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
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	
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	
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	
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	
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	
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	
Nausea			
subjects affected / exposed	6 / 698 (0.86%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	5 / 6	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			

subjects affected / exposed	5 / 698 (0.72%)	1 / 692 (0.14%)	
occurrences causally related to treatment / all	1 / 6	0 / 1	
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	
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	
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	
Stomatitis			
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	
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	
Vomiting			
subjects affected / exposed	6 / 698 (0.86%)	9 / 692 (1.30%)	
occurrences causally related to treatment / all	4 / 6	10 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
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	
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	
Biliary colic			
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	
Cholangitis			
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	
Cholecystitis			
subjects affected / exposed	4 / 698 (0.57%)	6 / 692 (0.87%)	
occurrences causally related to treatment / all	0 / 5	1 / 8	
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	
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	
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	
Gallbladder 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	
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	
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	
Skin and subcutaneous tissue disorders			
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	
Dermatitis exfoliative			
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	
Rash			
subjects affected / exposed	5 / 698 (0.72%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	3 / 5	0 / 2	
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	
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	
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			

Acute kidney injury			
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	
Acute prerenal failure			
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	
Dysuria			
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	
Hydronephrosis			
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	
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 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	
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	
Ureteric obstruction			

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	
Musculoskeletal and connective tissue disorders			
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	
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	
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	
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	
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	
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	
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	
Neck 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	
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	
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	
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	
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	
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	
Spinal column 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	
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	
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	
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	
Infections and infestations			
Abdominal 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	
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	
Appendicitis			
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	
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	
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	
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	
Bacteraemia			
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	
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	
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	
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	
Bronchitis			
subjects affected / exposed	7 / 698 (1.00%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	2 / 7	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Campylobacter 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	
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	
Cellulitis			
subjects affected / exposed	3 / 698 (0.43%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	1 / 3	2 / 3	
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 / 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	
Cytomegalovirus 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	
Device related infection			
subjects affected / exposed	2 / 698 (0.29%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	2 / 2	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	
Diverticulitis			

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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
Herpes zoster			
subjects affected / exposed	7 / 698 (1.00%)	8 / 692 (1.16%)	
occurrences causally related to treatment / all	4 / 7	4 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster disseminated			
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	
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	
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	
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	
Infection			
subjects affected / exposed	6 / 698 (0.86%)	8 / 692 (1.16%)	
occurrences causally related to treatment / all	2 / 7	2 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease			

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 / 1	0 / 0	
Influenza			
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	
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	
Lower respiratory tract infection			
subjects affected / exposed	12 / 698 (1.72%)	7 / 692 (1.01%)	
occurrences causally related to treatment / all	8 / 19	2 / 7	
deaths causally related to treatment / all	1 / 2	0 / 0	
Lung infection			
subjects affected / exposed	8 / 698 (1.15%)	6 / 692 (0.87%)	
occurrences causally related to treatment / all	4 / 12	6 / 6	
deaths causally related to treatment / all	1 / 2	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	
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	
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	
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	
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	
Neutropenic sepsis			
subjects affected / exposed	5 / 698 (0.72%)	5 / 692 (0.72%)	
occurrences causally related to treatment / all	6 / 7	7 / 8	
deaths causally related to treatment / all	0 / 0	0 / 1	
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	
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	
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	
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	
Pelvic 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	
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	
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	
Pharyngeal 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	
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	
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	
Pneumonia			
subjects affected / exposed	42 / 698 (6.02%)	30 / 692 (4.34%)	
occurrences causally related to treatment / all	18 / 45	14 / 35	
deaths causally related to treatment / all	1 / 5	0 / 2	
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	
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	
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	
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	
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	
Pyelonephritis			
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 tract infection			
subjects affected / exposed	5 / 698 (0.72%)	4 / 692 (0.58%)	
occurrences causally related to treatment / all	3 / 5	8 / 10	
deaths causally related to treatment / all	0 / 1	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	
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	
Sepsis			
subjects affected / exposed	13 / 698 (1.86%)	6 / 692 (0.87%)	
occurrences causally related to treatment / all	8 / 17	4 / 6	
deaths causally related to treatment / all	0 / 2	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	
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	
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	
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	
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	
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	
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	
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	
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	
Upper respiratory tract infection			
subjects affected / exposed	6 / 698 (0.86%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	2 / 8	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	9 / 698 (1.29%)	6 / 692 (0.87%)	
occurrences causally related to treatment / all	2 / 9	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	3 / 698 (0.43%)	3 / 692 (0.43%)	
occurrences causally related to treatment / all	3 / 4	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
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	
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	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	3 / 698 (0.43%)	2 / 692 (0.29%)	
occurrences causally related to treatment / all	2 / 3	1 / 2	
deaths causally related to treatment / all	1 / 1	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	
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	
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	
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	
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	
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	

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	679 / 698 (97.28%)	663 / 692 (95.81%)	
Vascular disorders			
Flushing			
subjects affected / exposed	46 / 698 (6.59%)	39 / 692 (5.64%)	
occurrences (all)	56	40	
Hypertension			

subjects affected / exposed	53 / 698 (7.59%)	45 / 692 (6.50%)	
occurrences (all)	74	61	
Hypotension			
subjects affected / exposed	40 / 698 (5.73%)	23 / 692 (3.32%)	
occurrences (all)	44	26	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	32 / 698 (4.58%)	36 / 692 (5.20%)	
occurrences (all)	38	45	
Chest discomfort			
subjects affected / exposed	42 / 698 (6.02%)	37 / 692 (5.35%)	
occurrences (all)	44	43	
Chills			
subjects affected / exposed	120 / 698 (17.19%)	71 / 692 (10.26%)	
occurrences (all)	162	91	
Fatigue			
subjects affected / exposed	259 / 698 (37.11%)	247 / 692 (35.69%)	
occurrences (all)	374	343	
Mucosal inflammation			
subjects affected / exposed	30 / 698 (4.30%)	40 / 692 (5.78%)	
occurrences (all)	35	51	
Oedema peripheral			
subjects affected / exposed	39 / 698 (5.59%)	33 / 692 (4.77%)	
occurrences (all)	41	40	
Pyrexia			
subjects affected / exposed	187 / 698 (26.79%)	141 / 692 (20.38%)	
occurrences (all)	245	209	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	194 / 698 (27.79%)	163 / 692 (23.55%)	
occurrences (all)	264	214	
Dyspnoea			
subjects affected / exposed	106 / 698 (15.19%)	84 / 692 (12.14%)	
occurrences (all)	122	97	
Oropharyngeal pain			

subjects affected / exposed occurrences (all)	76 / 698 (10.89%) 91	69 / 692 (9.97%) 82	
Productive cough subjects affected / exposed occurrences (all)	35 / 698 (5.01%) 41	27 / 692 (3.90%) 32	
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	36 / 698 (5.16%) 38	27 / 692 (3.90%) 29	
Insomnia subjects affected / exposed occurrences (all)	104 / 698 (14.90%) 123	78 / 692 (11.27%) 88	
Investigations Weight decreased subjects affected / exposed occurrences (all)	33 / 698 (4.73%) 35	38 / 692 (5.49%) 41	
Injury, poisoning and procedural complications Infusion related reaction subjects affected / exposed occurrences (all)	405 / 698 (58.02%) 681	333 / 692 (48.12%) 534	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	66 / 698 (9.46%) 73	49 / 692 (7.08%) 59	
Dysgeusia subjects affected / exposed occurrences (all)	60 / 698 (8.60%) 72	55 / 692 (7.95%) 60	
Headache subjects affected / exposed occurrences (all)	138 / 698 (19.77%) 208	114 / 692 (16.47%) 174	
Neuropathy peripheral subjects affected / exposed occurrences (all)	49 / 698 (7.02%) 59	48 / 692 (6.94%) 49	
Paraesthesia subjects affected / exposed occurrences (all)	56 / 698 (8.02%) 64	45 / 692 (6.50%) 60	

Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	55 / 698 (7.88%) 63	47 / 692 (6.79%) 50	
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	65 / 698 (9.31%) 77	65 / 692 (9.39%) 84	
Leukopenia subjects affected / exposed occurrences (all)	81 / 698 (11.60%) 193	80 / 692 (11.56%) 234	
Neutropenia subjects affected / exposed occurrences (all)	328 / 698 (46.99%) 801	285 / 692 (41.18%) 698	
Thrombocytopenia subjects affected / exposed occurrences (all)	84 / 698 (12.03%) 147	48 / 692 (6.94%) 71	
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	68 / 698 (9.74%) 84	68 / 692 (9.83%) 83	
Abdominal pain upper subjects affected / exposed occurrences (all)	52 / 698 (7.45%) 58	41 / 692 (5.92%) 45	
Constipation subjects affected / exposed occurrences (all)	239 / 698 (34.24%) 307	205 / 692 (29.62%) 283	
Diarrhoea subjects affected / exposed occurrences (all)	183 / 698 (26.22%) 275	150 / 692 (21.68%) 220	
Dyspepsia subjects affected / exposed occurrences (all)	59 / 698 (8.45%) 74	42 / 692 (6.07%) 47	
Nausea subjects affected / exposed occurrences (all)	330 / 698 (47.28%) 555	312 / 692 (45.09%) 534	
Stomatitis			

subjects affected / exposed	53 / 698 (7.59%)	50 / 692 (7.23%)	
occurrences (all)	71	66	
Vomiting			
subjects affected / exposed	160 / 698 (22.92%)	134 / 692 (19.36%)	
occurrences (all)	208	191	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	88 / 698 (12.61%)	75 / 692 (10.84%)	
occurrences (all)	92	76	
Dry skin			
subjects affected / exposed	38 / 698 (5.44%)	33 / 692 (4.77%)	
occurrences (all)	43	36	
Erythema			
subjects affected / exposed	37 / 698 (5.30%)	32 / 692 (4.62%)	
occurrences (all)	40	38	
Pruritus			
subjects affected / exposed	91 / 698 (13.04%)	89 / 692 (12.86%)	
occurrences (all)	109	107	
Rash			
subjects affected / exposed	113 / 698 (16.19%)	120 / 692 (17.34%)	
occurrences (all)	142	154	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	103 / 698 (14.76%)	88 / 692 (12.72%)	
occurrences (all)	122	110	
Back pain			
subjects affected / exposed	94 / 698 (13.47%)	108 / 692 (15.61%)	
occurrences (all)	117	135	
Bone pain			
subjects affected / exposed	36 / 698 (5.16%)	37 / 692 (5.35%)	
occurrences (all)	41	44	
Muscle spasms			
subjects affected / exposed	37 / 698 (5.30%)	36 / 692 (5.20%)	
occurrences (all)	42	43	
Myalgia			

subjects affected / exposed	47 / 698 (6.73%)	30 / 692 (4.34%)	
occurrences (all)	54	35	
Pain in extremity			
subjects affected / exposed	63 / 698 (9.03%)	56 / 692 (8.09%)	
occurrences (all)	71	67	
Infections and infestations			
Bronchitis			
subjects affected / exposed	43 / 698 (6.16%)	34 / 692 (4.91%)	
occurrences (all)	60	44	
Herpes zoster			
subjects affected / exposed	64 / 698 (9.17%)	39 / 692 (5.64%)	
occurrences (all)	68	44	
Lower respiratory tract infection			
subjects affected / exposed	54 / 698 (7.74%)	66 / 692 (9.54%)	
occurrences (all)	88	91	
Nasopharyngitis			
subjects affected / exposed	117 / 698 (16.76%)	120 / 692 (17.34%)	
occurrences (all)	178	183	
Oral herpes			
subjects affected / exposed	39 / 698 (5.59%)	36 / 692 (5.20%)	
occurrences (all)	46	40	
Respiratory tract infection			
subjects affected / exposed	35 / 698 (5.01%)	31 / 692 (4.48%)	
occurrences (all)	55	34	
Rhinitis			
subjects affected / exposed	46 / 698 (6.59%)	32 / 692 (4.62%)	
occurrences (all)	56	41	
Sinusitis			
subjects affected / exposed	67 / 698 (9.60%)	42 / 692 (6.07%)	
occurrences (all)	90	51	
Upper respiratory tract infection			
subjects affected / exposed	125 / 698 (17.91%)	119 / 692 (17.20%)	
occurrences (all)	175	164	
Urinary tract infection			
subjects affected / exposed	67 / 698 (9.60%)	57 / 692 (8.24%)	
occurrences (all)	97	84	

Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	87 / 698 (12.46%)	77 / 692 (11.13%)	
occurrences (all)	102	89	
Hypokalaemia			
subjects affected / exposed	44 / 698 (6.30%)	25 / 692 (3.61%)	
occurrences (all)	64	37	

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.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported