



Clinical trial results:

A Multicenter, Open-Label, Single-Arm, Phase IIIb, International Study Evaluating the Safety of Obinutuzumab Alone or in Combination with Chemotherapy in Patients with Previously Untreated or Relapsed/Refractory Chronic Lymphocytic Leukemia

Summary

EudraCT number	2013-000087-29
Trial protocol	IT DE ES FI LV SI IE PT EE GR SE PL SK BE LT FR
Global end of trial date	

Results information

Result version number	v1
This version publication date	06 January 2018
First version publication date	06 January 2018

Trial information

Trial identification

Sponsor protocol code	MO28543
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01905943
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. HoffmannLa Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH4070
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	29 December 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 December 2016
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of obinutuzumab alone or in combination with chemotherapy.

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	04 November 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	30 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 8
Country: Number of subjects enrolled	Belgium: 18
Country: Number of subjects enrolled	Brazil: 34
Country: Number of subjects enrolled	Bosnia and Herzegovina: 7
Country: Number of subjects enrolled	Canada: 69
Country: Number of subjects enrolled	Estonia: 10
Country: Number of subjects enrolled	Finland: 10
Country: Number of subjects enrolled	France: 137
Country: Number of subjects enrolled	Germany: 117
Country: Number of subjects enrolled	Greece: 27
Country: Number of subjects enrolled	Ireland: 18
Country: Number of subjects enrolled	Israel: 20
Country: Number of subjects enrolled	Italy: 81
Country: Number of subjects enrolled	Korea, Republic of: 9
Country: Number of subjects enrolled	Latvia: 10
Country: Number of subjects enrolled	Lithuania: 15
Country: Number of subjects enrolled	Mexico: 21
Country: Number of subjects enrolled	Poland: 37
Country: Number of subjects enrolled	Portugal: 18
Country: Number of subjects enrolled	Romania: 3
Country: Number of subjects enrolled	Russian Federation: 35
Country: Number of subjects enrolled	Serbia: 10

Country: Number of subjects enrolled	Slovakia: 15
Country: Number of subjects enrolled	Slovenia: 9
Country: Number of subjects enrolled	Spain: 67
Country: Number of subjects enrolled	Sweden: 16
Country: Number of subjects enrolled	Switzerland: 41
Country: Number of subjects enrolled	Thailand: 20
Country: Number of subjects enrolled	Turkey: 75
Country: Number of subjects enrolled	Macedonia, the former Yugoslav Republic of: 3
Country: Number of subjects enrolled	Egypt: 12
Worldwide total number of subjects	972
EEA total number of subjects	608

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)	434
From 65 to 84 years	523
85 years and over	15

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 195 centers in 31 countries.

Pre-assignment

Screening details:

A total of 1131 subjects were screened and 979 subjects were enrolled. Due to compliance issues a site in Romania was closed. Seven subjects were excluded from the analysis, because data integrity was impacted by the site's non-compliance. Hence, data analysis is reported for 972 enrolled subjects.

Period 1

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

Arms

Arm title	Obinutuzumab
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Arm description:

Subjects received obinutuzumab either alone as single agent, or in combination with chemotherapy (Fludarabine/Cyclophosphamide [FC], Bendamustine or Chlorambucil) at the investigator's discretion.

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

Dosage and administration details:

Obinutuzumab was administered by intravenous (i.v.) infusion at a dose of 1000 mg. A treatment cycle was defined as lasting 28 days.

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 milligram per millilitre square (mg/m^2) I.V. over 60 minutes once daily (QD) Day 1–2 in subjects previously untreated or 70 mg/m^2 I.V. over 60 minutes QD Day 1–2 in subjects with relapsed/refractory disease. In non-fit subjects only, investigators may opt at their own discretion to use lower initial doses of bendamustine, i.e., bendamustine 70 mg/m^2 in previously untreated subjects, and bendamustine 50 mg/m^2 in relapsed/refractory subjects (over 60 minutes qd Day 1–2 for each administration).

Investigational medicinal product name	Fludarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion, Powder for oral suspension
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Fludarabine 25 mg/m^2 I.V. over 30 minutes QD Day 1–3 or o.) QD Day 1–3 in fit subjects only.

Fludarabine 40 mg/m^2 per os (p.

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion, Powder for oral suspension
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Cyclophosphamide 250 mg/m² I.V. over 15-30 minutes qd Day 1-3 or Cyclophosphamide 250 mg/m² p.o. QD Day 1-3 in fit subjects only.

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

Dosage and administration details:

Chlorambucil 0.5 mg/kg p.o. qd on Day 1 and Day 15 in non-fit subjects only.

Number of subjects in period 1	Obinutuzumab
Started	972
Completed	0
Not completed	972
Adverse event, serious fatal	105
Disease progression	2
Adverse event, non-fatal	10
Ongoing in study	777
Withdrawal of consent	63
Renal cell carcinoma	1
Lost to follow-up	9
Investigator discretion	4
Moved away from site	1

Baseline characteristics

Reporting groups

Reporting group title	Overall Study
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Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	972	972	
Age categorical			
Units: Subjects			
18-64 years	434	434	
65-84 years	523	523	
>=85 years	15	15	
Age Continuous			
Units: years			
arithmetic mean	65.4		
standard deviation	± 10.94	-	
Sex: Female, Male			
Units: Subjects			
Female	355	355	
Male	617	617	

End points

End points reporting groups

Reporting group title	Obinutuzumab
Reporting group description: Subjects received obinutuzumab either alone as single agent, or in combination with chemotherapy (Fludarabine/Cyclophosphamide [FC], Bendamustine or Chlorambucil) at the investigator's discretion.	
Subject analysis set title	G mono: Previously Untreated Fit
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects with obinutuzumab monotherapy who were perviously untreated fit. Fit subjects were defined as having a total Cumulative Illness Rating Scale (CIRS) score ≤ 6 and creatinine clearance (CrCl) ≥ 70 millilitre per minute (mL/min).	
Subject analysis set title	G mono: Previously Untreated Unfit
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects with obinutuzumab monotherapy who were perviously untreated unfit. Non fit subjects were defined as having a CIRS score > 6 and/or CrCl < 70 mL/min.	
Subject analysis set title	G mono: Relapsed/refractory
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects with obinutuzumab monotherapy who had documented relapsed/refractory chronic lymphocytic leukemia (CLL).	
Subject analysis set title	G-Benda: Previously Untreated Fit
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects with obinutuzumab in combination with bendamustine who were previously untreated fit. Fit subjects were defined as having a total CIRS score ≤ 6 and CrCl ≥ 70 mL/min.	
Subject analysis set title	G-Benda: Previously Untreated Unfit
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects with obinutuzumab in combination with bendamustine who were perviously untreated unfit. Non fit subjects were defined as having a CIRS score > 6 and/or CrCl < 70 mL/min.	
Subject analysis set title	G-Benda: Relapsed/refractory
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects with obinutuzumab in combination with bendamustine who had documented relapsed/refractory chronic lymphocytic leukemia (CLL).	
Subject analysis set title	G-FC: Previously Untreated Fit
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects with obinutuzumab in combination with fludarabine and cyclophosphamide who were previously untreated fit. Fit subjects were defined as having a total CIRS score ≤ 6 and CrCl ≥ 70 mL/min.	
Subject analysis set title	G-FC: Previously Untreated Unfit
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects with obinutuzumab in combination with fludarabine and cyclophosphamide who were previously untreated unfit. Non fit subjects were defined as having a CIRS score > 6 and/or CrCl < 70 mL/min. This is a Protocol deviation: unfit subjects were incorrectly assigned to the G-FC treatment regimen.	
Subject analysis set title	G-FC: Relapsed/refractory
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects with obinutuzumab in combination with fludarabine and cyclophosphamide who had documented relapsed/refractory chronic lymphocytic leukemia (CLL).	

Subject analysis set title	G-Clb: Previously Untreated Fit
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects with obinutuzumab in combination with chlorambucil who were previously untreated fit. Fit subjects were defined as having a total CIRS score ≤ 6 and CrCl ≥ 70 mL/min. This is a Protocol deviation: a fit subject was incorrectly assigned to G-Clb treatment regimen.	
Subject analysis set title	G-Clb: Previously Untreated Unfit
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects with obinutuzumab in combination with chlorambucil who were perviously untreated unfit. Non fit subjects were defined as having a CIRS score > 6 and/or CrCl < 70 mL/min.	
Subject analysis set title	G-Clb: Relapsed/refractory
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects with obinutuzumab in chlorambucil who had documented relapsed/refractory chronic lymphocytic leukemia (CLL).	

Primary: Number of Subjects with Adverse Events (AEs)

End point title	Number of Subjects with Adverse Events (AEs) ^[1]
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. AEs, including AEs of Special Interest and AEs of Particular Interest, were reported based on the national cancer institute common terminology criteria for AEs, Version 4.0 (NCI-CTCAE, v4.0). Reported are the number of subjects with AEs, Grade 3-5 AEs, and Serious Adverse Events (SAEs). The safety population was defined as all subjects who have received at least one dose of study medication.	
End point type	Primary
End point timeframe:	
Baseline up to data base lock date at time of primary study completion (up to approximately 3 years)	
Notes:	

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

Justification: No statistical analyses were performed as this study has only one arm.

End point values	Obinutuzumab			
Subject group type	Reporting group			
Number of subjects analysed	972			
Units: subjects				
AEs	950			
Grade 3-5 AEs	780			
SAEs	516			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Adverse Events of Special Interest (AESIs)

End point title	Number of Subjects with Adverse Events of Special Interest (AESIs) ^[2]
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End point description:

The following AEs were defined as AESIs: AEs with the preferred term Tumour Lysis Syndrome (TLS), Infusion-Related Reactions (IRRs) defined as AEs that occurred during or within 24 hours of the completion of obinutuzumab infusion and were assessed as related to obinutuzumab by the Investigator, Infections defined as AEs from System Organ Class (SOC) "Infections and infestations" and AEs with the preferred term Neutropenia. The safety population was defined as all subjects who have received at least one dose of study medication.

End point type	Primary
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End point timeframe:

Baseline up to data base lock date at time of primary study completion (up to approximately 3 years)

Notes:

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

Justification: No statistical analyses were performed as this study has only one arm.

End point values	Obinutuzumab			
Subject group type	Reporting group			
Number of subjects analysed	971			
Units: subjects				
Total AESIs	895			
IRRs	635			
Neutropenia	599			
Infections	521			
TLS	62			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Adverse Events of Particular Interest (AEPIs)

End point title	Number of Subjects with Adverse Events of Particular Interest (AEPIs) ^[3]
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End point description:

The following AEs were defined as AEPIs: AEs with the preferred term Progressive multifocal leukoencephalopathy, hepatitis B reactivation defined as AEs with preferred term containing "Hepatitis B" or "hepatitis acute, thrombocytopenia defined via Roche MedDRA basket subgroup "haematopoietic thrombocytopenia", second malignancies defined as AEs from the SOC "Neoplasms benign, malignant and unspecified" starting 6 months after the first study drug intake, second malignancies based on standardised MedDRA queries (SMQ), starting 6 months after the first study drug intake based on the MedDRA SMQ "Malignant or unspecified tumours", in which benign neoplasms are not included, AEs from the SOC "Cardiac disorders" and hemorrhagic events defined via Roche MedDRA basket subgroup "Haemorrhagic events". The safety population was defined as all participants who have received at least one dose of study medication.

End point type	Primary
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End point timeframe:

Baseline up to data base lock date at time of primary study completion (up to approximately 3 years)

Notes:

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

Justification: No statistical analyses were performed as this study has only one arm.

End point values	Obinutuzumab			
Subject group type	Reporting group			
Number of subjects analysed	971			
Units: subjects				
Total AEPis	467			
Thrombocytopenia	314			
Cardiac events	109			
Second malignancies	82			
Second malignancies (SMQ)	75			
Hemorrhagic events	69			
Hepatitis B reactivation	3			
PML	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Minimal Residual Disease (MRD)-Negativity as Assessed by Flow Cytometry

End point title	Percentage of Subjects with Minimal Residual Disease (MRD)-Negativity as Assessed by Flow Cytometry
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End point description:

MRD-negativity was defined as the presence of less than 1 chronic lymphocytic leukemia (CLL) cell per 10,000 leukocytes, as assessed by flow cytometry 3 months after the last dose of study treatment (i.e. at final response assessment visit). The MRD intent-to-ship (ITS) population included all subjects whose shipment of fresh blood to the central laboratory for purpose of MRD analyses could occur within 48 hours. MRD ITS population was a part of the intent-to-treat population. Number of subjects analyzed indicates subjects who took part in the analysis.

End point type	Secondary
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End point timeframe:

3 months after the last dose of study treatment (up to approximately 5 years)

End point values	G mono: Previously Untreated Fit	G mono: Previously Untreated Unfit	G mono: Relapsed/refra ctory	G-Benda: Previously Untreated Fit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24 ^[4]	26 ^[5]	48 ^[6]	148 ^[7]
Units: percentage of subjects				
number (not applicable)				
Blood	8.3	23.1	4.2	62.8
Bone marrow	4.2	3.8	2.1	31.8

Notes:

[4] - Number of subjects analysed for this endpoint.

[5] - Number of subjects analysed for this endpoint.

[6] - Number of subjects analysed for this endpoint.

[7] - Number of subjects analysed for this endpoint.

End point values	G-Benda: Previously	G-Benda: Relapsed/refra	G-FC: Previously	G-FC: Previously
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	Untreated Unfit	Untreated Fit	Untreated Unfit	Untreated Unfit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	148 ^[8]	162 ^[9]	125 ^[10]	12 ^[11]
Units: percentage of subjects				
number (not applicable)				
Blood	64.9	39.5	72.0	58.3
Bone marrow	27.0	14.8	40.0	41.7

Notes:

[8] - Number of subjects analysed for this endpoint.

[9] - Number of subjects analysed for this endpoint.

[10] - Number of subjects analysed for this endpoint.

[11] - Number of subjects analysed for this endpoint.

End point values	G-FC: Relapsed/refractory	G-Clb: Previously Untreated Fit	G-Clb: Previously Untreated Unfit	G-Clb: Relapsed/refractory
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	33 ^[12]	0 ^[13]	53 ^[14]	32 ^[15]
Units: percentage of subjects				
number (not applicable)				
Blood	51.5		9.4	6.3
Bone marrow	24.2		5.7	3.1

Notes:

[12] - Number of subjects analysed for this endpoint.

[13] - No subject was analysed for the reporting group G-clb: previously untreated fit

[14] - Number of subjects analysed for this endpoint.

[15] - Number of subjects analysed for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Overall Response (OR) at Final Response Assessment (FRA)

End point title	Percentage of Subjects with Overall Response (OR) at Final Response Assessment (FRA)
End point description:	
OR: percentage of subjects with complete response (CR) or CR with incomplete marrow recovery (CRi), or partial response (PR), determined by investigator based on International Workshop on Chronic Lymphocytic Leukemia (IWCLL) tumour response criteria. CR: Peripheral blood lymphocytes 4,000/mcL, no significant lymphadenopathy, no hepatomegaly and splenomegaly, no disease symptoms, blood counts: neutrophils >1,500/mcL, platelets > 100,000/mcL, hemoglobin(Hb)> 110 g/L and bone marrow normocellular for age. Cri: CR with persistent cytopenia. PR:>= 50% decrease in peripheral blood lymphocyte count AND >= 50% reduction in lymphadenopathy OR >= 50% reduction of liver enlargement OR >= 50% reduction of spleen PLUS one of the following: neutrophils >1,500/mcL, platelets > 100,000/mcL, Hb > 110 g/L OR >= 50% increase in neutrophils, platelets or Hb. ITT population was defined as all subjects enrolled in the study regardless of whether or not they received any study drug.	
End point type	Secondary
End point timeframe:	
3 months after the last dose of study treatment (up to approximately 5 years)	

End point values	G mono: Previously Untreated Fit	G mono: Previously Untreated Unfit	G mono: Relapsed/refra ctory	G-Benda: Previously Untreated Fit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	31	32	64	167
Units: percentage of subjects				
number (confidence interval 95%)	71 (52 to 85.8)	56.3 (37.7 to 73.6)	42.2 (29.9 to 55.2)	83.8 (77.4 to 89.1)

End point values	G-Benda: Previously Untreated Unfit	G-Benda: Relapsed/refra ctory	G-FC: Previously Untreated Fit	G-FC: Previously Untreated Unfit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	180	191	140	13
Units: percentage of subjects				
number (confidence interval 95%)	80 (73.4 to 85.6)	72.8 (65.9 to 79.0)	90 (83.8 to 94.4)	84.6 (54.6 to 98.1)

End point values	G-FC: Relapsed/refra ctory	G-Clb: Previously Untreated Fit	G-Clb: Previously Untreated Unfit	G-Clb: Relapsed/refra ctory
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	40	1	67	46
Units: percentage of subjects				
number (confidence interval 95%)	82.5 (67.2 to 92.7)	100 (2.5 to 100)	82.1 (70.8 to 90.4)	54.3 (39.0 to 69.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS)
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End point description:

PFS was defined as time from the date of enrollment until the first documented progressive disease (PD) based on IWCLL tumor response criteria or death from any cause, whichever occurred first. PD: at least one of the following: $\geq 50\%$ increase in the absolute number of circulating lymphocytes to at least 5,000/mcL, appearance of new palpable lymph nodes, $\geq 50\%$ increase in the longest diameter of any previous site of clinically significant lymphadenopathy, $\geq 50\%$ increase in the enlargement of the liver and/or spleen, transformation to more aggressive histology, progression of any cytopenia, decrease of Hb levels by > 20 g/L or to less than 100 g/L, decrease of platelet counts by $> 50\%$ or to $< 100,000$ /mcL, decrease of neutrophil counts by $> 50\%$ or to $< 1,000$ /mcL. The ITT population was defined as all subjects enrolled in the study regardless of whether or not they received any study drug. 9.9999 = PFS event not reached at time of analysis.

End point type	Secondary
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End point timeframe:

Baseline, Day 85, end of treatment or early termination, and follow-up, assessed up to disease progression or death, whichever occurs first (up to approximately 5 years)

End point values	G mono: Previously Untreated Fit	G mono: Previously Untreated Unfit	G mono: Relapsed/refra ctory	G-Benda: Previously Untreated Fit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	31	32	64	167
Units: months				
median (full range (min-max))	9.9999 (0.0 to 33.8)	9.9999 (0.0 to 33.6)	17.6 (0.0 to 34.1)	9.9999 (0.0 to 36.7)

End point values	G-Benda: Previously Untreated Unfit	G-Benda: Relapsed/refra ctory	G-FC: Previously Untreated Fit	G-FC: Previously Untreated Unfit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	180	191	140	13
Units: months				
median (full range (min-max))	9.9999 (0.0 to 36.2)	25.8 (0.0 to 35.7)	9.9999 (0.0 to 36.7)	9.9999 (1.1 to 33.4)

End point values	G-FC: Relapsed/refra ctory	G-Clb: Previously Untreated Fit	G-Clb: Previously Untreated Unfit	G-Clb: Relapsed/refra ctory
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	40	0 ^[16]	67	46
Units: months				
median (full range (min-max))	28.1 (2.5 to 33.9)	(to)	27.5 (0.0 to 34.4)	14.1 (0.0 to 30.6)

Notes:

[16] - PFS not reached at time of analysis. Full range 21.4 to 21.4.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response (TTR)

End point title	Time to Response (TTR)
End point description:	
TTR was defined as the interval from the date of enrollment to the first documentation of CR or PR based on IWCLL tumor response criteria. CR: Peripheral blood lymphocytes 4,000/mcL, no significant lymphadenopathy, no hepatomegaly and splenomegaly, no disease symptoms, blood counts: neutrophils >1,500/mcL, platelets > 100,000/mcL, hemoglobin > 110 g/L and bone marrow normocellular for age. PR: >/= 50% decrease in peripheral blood lymphocyte count AND >/= 50% reduction in lymphadenopathy OR >/= 50% reduction of liver enlargement OR >/= 50% reduction of spleen PLUS one of the following: neutrophils >1,500/mcL, platelets > 100,000/mcL, hemoglobin > 110 g/L OR >/= 50% increase in neutrophils, platelets or hemoglobin. The ITT population was defined as all subjects enrolled in the study regardless of whether or not they received any study drug.	
End point type	Secondary

End point timeframe:

Baseline, Day 85, end of treatment or early termination, and follow-up, assessed up to disease progression or death, whichever occurs first (up to approximately 5 years)

End point values	G mono: Previously Untreated Fit	G mono: Previously Untreated Unfit	G mono: Relapsed/refra ctory	G-Benda: Previously Untreated Fit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	31	32	64	167
Units: months				
median (full range (min-max))	3.6 (0.9 to 10.5)	3.6 (0.1 to 33.6)	3.9 (0.2 to 34.1)	3.5 (0.0 to 27.3)

End point values	G-Benda: Previously Untreated Unfit	G-Benda: Relapsed/refra ctory	G-FC: Previously Untreated Fit	G-FC: Previously Untreated Unfit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	180	191	140	13
Units: months				
median (full range (min-max))	3.5 (0.1 to 30.3)	3.7 (0.0 to 33.6)	3.6 (0.1 to 19.6)	4.1 (1.1 to 19.0)

End point values	G-FC: Relapsed/refra ctory	G-Clb: Previously Untreated Fit	G-Clb: Previously Untreated Unfit	G-Clb: Relapsed/refra ctory
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	40	1	67	46
Units: months				
median (full range (min-max))	3.6 (1.1 to 9.0)	3.3 (3.3 to 3.3)	3.6 (0.2 to 16.6)	3.7 (0.1 to 16.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Event-Free Survival (EFS)

End point title	Event-Free Survival (EFS)
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End point description:

EFS: time from enrollment to first event of PD or relapse, as assessed by the investigator based on IWCLL criteria, or start of a non-protocol-specified anti-leukemia therapy or death, whichever occurs first. PD: at least one of the following: $\geq 50\%$ increase in the absolute number of circulating lymphocytes to at least 5,000/mcL, appearance of new palpable lymph nodes, $\geq 50\%$ increase in the longest diameter of any previous site of clinically significant lymphadenopathy, $\geq 50\%$ increase in the enlargement of the liver and/or spleen, transformation to more aggressive histology, progression of any cytopenia, decrease of hemoglobin levels by more than 20 g/L or to less than 100 g/L, decrease of platelet counts by more than 50% or to $< 100,000$ /mcL, decrease of neutrophil counts by $> 50\%$ or to

< 1,000/mcL. The ITT population was defined as all subjects enrolled in the study regardless of whether or not they received any study drug. 9.9999 = EFS event not reached at time of analysis.

End point type	Secondary
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End point timeframe:

Baseline, Day 85, end of treatment or early termination, and follow-up, assessed up to disease progression or death, whichever occurs first (up to approximately 5 years)

End point values	G mono: Previously Untreated Fit	G mono: Previously Untreated Unfit	G mono: Relapsed/refra ctory	G-Benda: Previously Untreated Fit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	31	32	64	167
Units: months				
median (full range (min-max))	30.2 (0.0 to 33.8)	17.0 (0.0 to 33.6)	14.4 (0.0 to 33.6)	9.9999 (0.0 to 36.7)

End point values	G-Benda: Previously Untreated Unfit	G-Benda: Relapsed/refra ctory	G-FC: Previously Untreated Fit	G-FC: Previously Untreated Unfit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	180	191	140	13
Units: months				
median (full range (min-max))	9.9999 (0.0 to 36.2)	25.0 (0.0 to 35.7)	9.9999 (0.0 to 36.7)	9.9999 (1.1 to 33.4)

End point values	G-FC: Relapsed/refra ctory	G-Clb: Previously Untreated Fit	G-Clb: Previously Untreated Unfit	G-Clb: Relapsed/refra ctory
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	40	0 ^[17]	67	46
Units: months				
median (full range (min-max))	24.8 (2.0 to 33.9)	(to)	27.5 (0.0 to 34.4)	13.7 (0.3 to 30.6)

Notes:

[17] - EFS event not reached at time of analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Best Overall Response (BOR)

End point title	Percentage of Subjects with Best Overall Response (BOR)
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End point description:

BOR was defined as percentage of subjects with best response obtained throughout the trial with CR, CRi, or PR, as determined by the investigator according to IWCLL tumor response criteria. CR: Peripheral blood lymphocytes 4,000/mcL, no significant lymphadenopathy, no hepatomegaly and splenomegaly, no disease symptoms, blood counts: neutrophils > 1,500/mcL, platelets > 100,000/mcL, hemoglobin > 110 g/L and bone marrow normocellular for age. Cri: CR with persistent cytopenia. PR:

$\geq 50\%$ decrease in peripheral blood lymphocyte count AND $\geq 50\%$ reduction in lymphadenopathy OR $\geq 50\%$ reduction of liver enlargement OR $\geq 50\%$ reduction of spleen PLUS one of the following: neutrophils $> 1,500/\text{mL}$, platelets $> 100,000/\text{mL}$, Hb $> 110 \text{ g/L}$ OR $\geq 50\%$ increase in neutrophils, platelets or Hb. ITT population was defined as all subjects enrolled in the study regardless of whether or not they received any study drug. Number of subjects analysed indicates subjects who took part in the analysis.

End point type	Secondary
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End point timeframe:

Baseline, Day 85, end of treatment or early termination, and follow-up, assessed up to disease progression or death, whichever occurs first (up to approximately 5 years)

End point values	G mono: Previously Untreated Fit	G mono: Previously Untreated Unfit	G mono: Relapsed/refractory	G-Benda: Previously Untreated Fit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	31	32	64	167
Units: percentage of subjects				
number (confidence interval 95%)	83.9 (66.3 to 94.5)	71.9 (53.3 to 86.3)	62.5 (49.5 to 74.3)	92.2 (87.1 to 95.8)

End point values	G-Benda: Previously Untreated Unfit	G-Benda: Relapsed/refractory	G-FC: Previously Untreated Fit	G-FC: Previously Untreated Unfit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	180	191	140	13
Units: percentage of subjects				
number (confidence interval 95%)	93.3 (88.6 to 96.5)	86.4 (80.7 to 90.9)	95.7 (90.9 to 98.4)	84.6 (54.6 to 98.1)

End point values	G-FC: Relapsed/refractory	G-Clb: Previously Untreated Fit	G-Clb: Previously Untreated Unfit	G-Clb: Relapsed/refractory
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	40	1	67	46
Units: percentage of subjects				
number (confidence interval 95%)	97.5 (86.8 to 99.9)	100 (2.5 to 100)	92.5 (83.4 to 97.5)	84.8 (71.1 to 93.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) Event

End point title	Overall Survival (OS) Event
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End point description:

OS was defined as the time from the date of enrollment until the date of death, regardless of the cause

of death. The ITT population was defined as all subjects enrolled in the study regardless of whether or not they received any study drug. 9.9999 = OS event not reached at time of analysis.

End point type	Secondary
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End point timeframe:

Baseline until death (Approximately up to 5 years)

End point values	G mono: Previously Untreated Fit	G mono: Previously Untreated Unfit	G mono: Relapsed/refra ctory	G-Benda: Previously Untreated Fit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	31	32	64	167
Units: months				
median (full range (min-max))	9.9999 (1.4 to 34.1)	9.9999 (0.6 to 36.7)	9.9999 (0.4 to 36.4)	9.9999 (0.5 to 37.5)

End point values	G-Benda: Previously Untreated Unfit	G-Benda: Relapsed/refra ctory	G-FC: Previously Untreated Fit	G-FC: Previously Untreated Unfit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	180	191	140	13
Units: months				
median (full range (min-max))	9.9999 (1.0 to 37.3)	9.9999 (1.6 to 37.5)	9.9999 (2.0 to 37.8)	9.9999 (1.1 to 36.4)

End point values	G-FC: Relapsed/refra ctory	G-Clb: Previously Untreated Fit	G-Clb: Previously Untreated Unfit	G-Clb: Relapsed/refra ctory
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	40	0 ^[18]	67	46
Units: months				
median (full range (min-max))	9.9999 (2.5 to 37.3)	(to)	9.9999 (2.0 to 36.5)	9.9999 (0.3 to 34.1)

Notes:

[18] - OS not reached at time of analysis. Full range 22.3 to 22.3

Statistical analyses

No statistical analyses for this end point

Secondary: Time to New Anti-Leukemia Therapy (TTNT)

End point title	Time to New Anti-Leukemia Therapy (TTNT)
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End point description:

TTNT was defined as the time between the date of enrollment and first intake of new anti-leukemia therapy. The ITT population was defined as all subjects enrolled in the study regardless of whether or not they received any study drug. 9.9999 = TTNT event not reached at time of analysis.

End point type	Secondary
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End point timeframe:

Baseline until end of study (up to approximately 5 years)

End point values	G mono: Previously Untreated Fit	G mono: Previously Untreated Unfit	G mono: Relapsed/refractory	G-Benda: Previously Untreated Fit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	31	32	64	167
Units: months				
median (full range (min-max))	33.2 (1.4 to 34.3)	9.9999 (0.5 to 34.6)	22.1 (0.3 to 36.4)	9.9999 (0.3 to 37.5)

End point values	G-Benda: Previously Untreated Unfit	G-Benda: Relapsed/refractory	G-FC: Previously Untreated Fit	G-FC: Previously Untreated Unfit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	180	191	140	13
Units: months				
median (full range (min-max))	9.9999 (1.0 to 37.3)	9.9999 (1.4 to 37.5)	9.9999 (1.2 to 37.8)	9.9999 (1.1 to 36.4)

End point values	G-FC: Relapsed/refractory	G-Clb: Previously Untreated Fit	G-Clb: Previously Untreated Unfit	G-Clb: Relapsed/refractory
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	40	0 ^[19]	67	46
Units: months				
median (full range (min-max))	32.4 (2.0 to 37.3)	(to)	9.9999 (2.0 to 36.5)	20.4 (0.3 to 34.1)

Notes:

[19] - TTNT not reached at time of analysis. Full range 22.3 to 22.3.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR)

End point title	Duration of Response (DoR)
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End point description:

DoR was defined as the period from the date of initial confirmed PR or CR until the date of PD or death from any cause. PR: $\geq 50\%$ decrease in peripheral blood lymphocyte count AND $\geq 50\%$ reduction in lymphadenopathy OR $\geq 50\%$ reduction of liver enlargement OR $\geq 50\%$ reduction of spleen PLUS one of the following: neutrophils $>1,500/\text{mcL}$, platelets $>100,000/\text{mcL}$, hemoglobin $>110 \text{ g/L}$ OR $\geq 50\%$ increase in neutrophils, platelets or hemoglobin. CR: Peripheral blood lymphocytes $4,000/\text{mcL}$, no significant lymphadenopathy, no hepatomegaly and splenomegaly, no disease symptoms, blood counts: neutrophils $>1,500/\text{mcL}$, platelets $>100,000/\text{mcL}$, hemoglobin $>110 \text{ g/L}$ and bone marrow normocellular for age. PD: as defined in the description for Event-Free Survival outcome measure. The ITT population was defined as all subjects enrolled in the study regardless of whether or not they

received any study drug. 9.9999 = event not reached at time of analysis.

End point type	Secondary
End point timeframe:	
Baseline, Day 85, end of treatment or early termination, and follow-up, assessed up to disease progression or death, whichever occurs first (up to approximately 5 years)	

End point values	G mono: Previously Untreated Fit	G mono: Previously Untreated Unfit	G mono: Relapsed/refra ctory	G-Benda: Previously Untreated Fit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	26 ^[20]	23 ^[21]	40 ^[22]	154 ^[23]
Units: months				
median (full range (min-max))	26.3 (0.0 to 30.2)	9.9999 (0.0 to 30.3)	15.7 (0.6 to 29.9)	9.999 (0.0 to 33.2)

Notes:

[20] - Number of subjects analysed for this endpoint.

[21] - Number of subjects analysed for this endpoint.

[22] - Number of subjects analysed for this endpoint.

[23] - Number of subjects analysed for this endpoint.

End point values	G-Benda: Previously Untreated Unfit	G-Benda: Relapsed/refra ctory	G-FC: Previously Untreated Fit	G-FC: Previously Untreated Unfit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	168 ^[24]	165 ^[25]	134 ^[26]	11 ^[27]
Units: months				
median (full range (min-max))	9.9999 (0.0 to 33.0)	24.1 (0.0 to 32.7)	9.9999 (0.0 to 33.4)	9.9999 (7.8 to 30.1)

Notes:

[24] - Number of subjects analysed for this endpoint.

[25] - Number of subjects analysed for this endpoint.

[26] - Number of subjects analysed for this endpoint.

[27] - Number of subjects analysed for this endpoint.

End point values	G-FC: Relapsed/refra ctory	G-Clb: Previously Untreated Fit	G-Clb: Previously Untreated Unfit	G-Clb: Relapsed/refra ctory
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	39 ^[28]	0 ^[29]	62 ^[30]	39 ^[31]
Units: months				
median (full range (min-max))	21.2 (0.0 to 30.7)	(to)	24.0 (0.0 to 30.3)	14.4 (1.4 to 27.0)

Notes:

[28] - Number of subjects analysed for this endpoint.

[29] - Event not reached at time of analysis.

Full range: 18.2 to 18.2

[30] - Number of subjects analysed for this endpoint.

[31] - Number of subjects analysed for this endpoint.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline to data cut-off date 29 Dec 2016 (up to 3 years)

Adverse event reporting additional description:

The safety population was defined as all subjects who have received at least one dose of study medication. AEs that were entered into the database at the time of the database lock were included in the AE analysis. A small set of AEs was not included and will be included at the time of final analysis.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.1
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Reporting groups

Reporting group title	G-Mono
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Reporting group description:

Subjects received obinutuzumab either alone as single agent.

Reporting group title	G-FC
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Reporting group description:

Subjects received obinutuzumab either alone as single agent, or in combination fludarabine/cyclophosphamide [FC] at the investigator's discretion.

Reporting group title	G-Clb
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Reporting group description:

Subjects received obinutuzumab either alone as single agent, or in combination with chlorambucil at the investigator's discretion.

Reporting group title	G-Benda
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Reporting group description:

Subjects received obinutuzumab in combination with bendamustine at the investigator's discretion.

Serious adverse events	G-Mono	G-FC	G-Clb
Total subjects affected by serious adverse events			
subjects affected / exposed	67 / 126 (53.17%)	87 / 193 (45.08%)	57 / 114 (50.00%)
number of deaths (all causes)	11	9	9
number of deaths resulting from adverse events	0	2	4
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 126 (0.79%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder transitional cell carcinoma			

subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cholangiocarcinoma			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clear cell renal cell carcinoma			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastatic carcinoma of the bladder			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Richter's syndrome			
subjects affected / exposed	1 / 126 (0.79%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Spinal meningioma benign			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma			

subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma gastric			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenosquamous cell lung cancer			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	2 / 114 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder cancer stage 0, with cancer in situ			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bowen's disease			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myeloid leukaemia			
subjects affected / exposed	0 / 126 (0.00%)	2 / 193 (1.04%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Breast cancer			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastatic renal cell carcinoma			

subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelodysplastic syndrome			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	2 / 114 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasal cavity cancer			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Primary myelofibrosis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal adenocarcinoma			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial carcinoma			

subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial cancer			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatocellular carcinoma			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal cancer			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma metastatic			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung cancer metastatic			

subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastatic bronchial carcinoma			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastatic malignant melanoma			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastatic squamous cell carcinoma			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelofibrosis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm malignant			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma metastatic			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatic adenoma			

subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin cancer			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small cell lung cancer metastatic			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 126 (1.59%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	4 / 126 (3.17%)	1 / 193 (0.52%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	4 / 4	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery thrombosis			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flushing			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			

subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral vascular disorder			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock haemorrhagic			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vena cava thrombosis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis superficial			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 126 (0.79%)	1 / 193 (0.52%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 1
Device related thrombosis			

subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	3 / 126 (2.38%)	11 / 193 (5.70%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	1 / 6	6 / 11	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chills			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Euthanasia			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthermia			

subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	3 / 126 (2.38%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytokine release syndrome			
subjects affected / exposed	5 / 126 (3.97%)	2 / 193 (1.04%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	5 / 5	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Allergy to immunoglobulin therapy			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug hypersensitivity			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	0 / 126 (0.00%)	3 / 193 (1.55%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	3 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune disorder			

subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 126 (1.59%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiectasis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chylothorax			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			

subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obliterative bronchiolitis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngeal inflammation			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			

subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary necrosis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory alkalosis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspiration			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Organising pneumonia			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Oropharyngeal pain			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Alcohol withdrawal syndrome			

subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oxygen saturation decreased			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood pressure increased			

subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 126 (0.00%)	2 / 193 (1.04%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical vertebral fracture			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Craniocerebral injury			

subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	2 / 114 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiation skin injury			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			

subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Radiation mucositis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	3 / 126 (2.38%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus bradycardia			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			

subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve incompetence			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve incompetence			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			

subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Ventricular arrhythmia			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular extrasystoles			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular tachycardia			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Cardiopulmonary failure			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nervous system disorders			
Haemorrhage intracranial			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraparesis			

subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tremor			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Balance disorder			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haematoma			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			

subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Central nervous system lesion			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle spasticity			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 126 (1.59%)	3 / 193 (1.55%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 2	1 / 3	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune haemolytic anaemia			
subjects affected / exposed	2 / 126 (1.59%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			

subjects affected / exposed	6 / 126 (4.76%)	20 / 193 (10.36%)	2 / 114 (1.75%)
occurrences causally related to treatment / all	2 / 6	11 / 22	2 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Haemolytic anaemia			
subjects affected / exposed	1 / 126 (0.79%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	9 / 126 (7.14%)	28 / 193 (14.51%)	6 / 114 (5.26%)
occurrences causally related to treatment / all	6 / 10	38 / 49	7 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	2 / 126 (1.59%)	7 / 193 (3.63%)	5 / 114 (4.39%)
occurrences causally related to treatment / all	0 / 2	5 / 7	5 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 126 (0.00%)	2 / 193 (1.04%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphopenia			
subjects affected / exposed	0 / 126 (0.00%)	2 / 193 (1.04%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bicytopenia			

subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal detachment			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			

subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticular perforation			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mouth haemorrhage			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritoneal adhesions			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			

subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic colitis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	1 / 126 (0.79%)	2 / 193 (1.04%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 1	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	2 / 126 (1.59%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hepatocellular injury			
subjects affected / exposed	2 / 126 (1.59%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute hepatic failure			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			

subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis toxic			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver disorder			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatitis allergic			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Purpura			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic foot			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			

subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug eruption			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive nephropathy			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			

subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral prolapse			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hypercalcaemia of malignancy			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperparathyroidism			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthyroidism			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Fistula inflammation			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid arthritis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal column stenosis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal pain			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial sepsis			

subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	2 / 126 (1.59%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal sepsis			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fungal infection			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	1 / 126 (0.79%)	2 / 193 (1.04%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			

subjects affected / exposed	1 / 126 (0.79%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 126 (0.79%)	2 / 193 (1.04%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	3 / 114 (2.63%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oropharyngeal candidiasis			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	11 / 126 (8.73%)	13 / 193 (6.74%)	16 / 114 (14.04%)
occurrences causally related to treatment / all	1 / 11	6 / 14	8 / 17
deaths causally related to treatment / all	0 / 1	0 / 2	2 / 3
Pneumonia viral			
subjects affected / exposed	1 / 126 (0.79%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Progressive multifocal leukoencephalopathy			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 126 (0.79%)	4 / 193 (2.07%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 1	3 / 4	0 / 2
deaths causally related to treatment / all	0 / 1	1 / 2	0 / 0
Septic shock			

subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheobronchitis			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	2 / 114 (1.75%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	1 / 126 (0.79%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal sepsis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			

subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute hepatitis B			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis infective			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspergillus infection			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain abscess			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis bacterial			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Campylobacter gastroenteritis			

subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Campylobacter infection			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium colitis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cryptosporidiosis infection			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			

subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear infection			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eczema infected			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis viral			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia bacteraemia			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Giardiasis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
H1N1 influenza			

subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster oticus			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected skin ulcer			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis B			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infective exacerbation chronic obstructive airways disease			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	0 / 126 (0.00%)	3 / 193 (1.55%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphangitis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis cryptococcal			

subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myringitis bullous			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasopharyngitis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis			
subjects affected / exposed	0 / 126 (0.00%)	2 / 193 (1.04%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral candidiasis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perirectal abscess			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia cytomegaloviral			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia pseudomonal			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomembranous colitis			

subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomonal sepsis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic abscess			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Visceral leishmaniasis			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
West nile viral infection			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			

subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia infection			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fungal oesophagitis			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral toxoplasmosis			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes virus infection			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis viral			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Listeriosis			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumococcal sepsis			

subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia fungal			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia pneumococcal			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinitis viral			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella zoster virus infection			
subjects affected / exposed	0 / 126 (0.00%)	2 / 193 (1.04%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection pseudomonal			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	2 / 114 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			

subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection enterococcal			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Tumour lysis syndrome			
subjects affected / exposed	1 / 126 (0.79%)	3 / 193 (1.55%)	3 / 114 (2.63%)
occurrences causally related to treatment / all	1 / 1	3 / 3	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 126 (0.00%)	1 / 193 (0.52%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperuricaemia			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malnutrition			

subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fluid overload			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 126 (0.00%)	0 / 193 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	G-Benda		
Total subjects affected by serious adverse events			
subjects affected / exposed	305 / 538 (56.69%)		
number of deaths (all causes)	45		
number of deaths resulting from adverse events	11		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	2 / 538 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bladder transitional cell carcinoma			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholangiocarcinoma			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Clear cell renal cell carcinoma subjects affected / exposed	0 / 538 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastatic carcinoma of the bladder subjects affected / exposed	0 / 538 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Richter's syndrome subjects affected / exposed	2 / 538 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Spinal meningioma benign subjects affected / exposed	0 / 538 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma subjects affected / exposed	6 / 538 (1.12%)			
occurrences causally related to treatment / all	5 / 9			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of skin subjects affected / exposed	4 / 538 (0.74%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			
Adenocarcinoma subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Adenocarcinoma gastric subjects affected / exposed	3 / 538 (0.56%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 1			
Adenosquamous cell lung cancer				

subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Basal cell carcinoma				
subjects affected / exposed	7 / 538 (1.30%)			
occurrences causally related to treatment / all	3 / 8			
deaths causally related to treatment / all	0 / 0			
Bladder cancer stage 0, with cancer in situ				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bowen's disease				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute myeloid leukaemia				
subjects affected / exposed	0 / 538 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Breast cancer				
subjects affected / exposed	0 / 538 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastatic renal cell carcinoma				
subjects affected / exposed	0 / 538 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myelodysplastic syndrome				
subjects affected / exposed	2 / 538 (0.37%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 1			
Prostate cancer				

subjects affected / exposed	3 / 538 (0.56%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Colon cancer			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malignant melanoma			
subjects affected / exposed	2 / 538 (0.37%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Nasal cavity cancer			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Primary myelofibrosis			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rectal adenocarcinoma			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchial carcinoma			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Chronic myeloid leukaemia			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endometrial cancer			

subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatocellular carcinoma				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intraductal proliferative breast lesion				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Laryngeal cancer				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung adenocarcinoma				
subjects affected / exposed	2 / 538 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Lung adenocarcinoma metastatic				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Lung cancer metastatic				
subjects affected / exposed	2 / 538 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Lung neoplasm malignant				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metastatic bronchial carcinoma				

subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metastatic malignant melanoma				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metastatic squamous cell carcinoma				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Myelofibrosis				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neoplasm malignant				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Pancreatic carcinoma metastatic				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Prostatic adenoma				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin cancer				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Small cell lung cancer metastatic				

subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 538 (0.37%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	4 / 538 (0.74%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral artery thrombosis			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Flushing			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Haematoma			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertensive crisis			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Orthostatic hypotension			

subjects affected / exposed	2 / 538 (0.37%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Peripheral vascular disorder			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Shock haemorrhagic			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vena cava thrombosis			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombophlebitis superficial			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Device related thrombosis			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			
subjects affected / exposed	2 / 538 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Malaise			

subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	21 / 538 (3.90%)			
occurrences causally related to treatment / all	10 / 25			
deaths causally related to treatment / all	0 / 0			
Asthenia				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chest pain				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chills				
subjects affected / exposed	4 / 538 (0.74%)			
occurrences causally related to treatment / all	5 / 5			
deaths causally related to treatment / all	0 / 0			
Euthanasia				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Hyperthermia				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Multiple organ dysfunction syndrome				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Oedema peripheral				

subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cytokine release syndrome			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Allergy to immunoglobulin therapy			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Drug hypersensitivity			
subjects affected / exposed	4 / 538 (0.74%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Hypersensitivity			
subjects affected / exposed	2 / 538 (0.37%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Autoimmune disorder			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Pulmonary oedema				
subjects affected / exposed	2 / 538 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Bronchiectasis				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chylothorax				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cough				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Interstitial lung disease				
subjects affected / exposed	2 / 538 (0.37%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 1			
Lung disorder				
subjects affected / exposed	2 / 538 (0.37%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Obliterative bronchiolitis				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pharyngeal inflammation				

subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	3 / 538 (0.56%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Pleurisy			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia aspiration			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pneumonitis			
subjects affected / exposed	2 / 538 (0.37%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pulmonary embolism			
subjects affected / exposed	4 / 538 (0.74%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 1		
Pulmonary necrosis			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory alkalosis			

subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Aspiration			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Organising pneumonia			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oropharyngeal pain			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Alcohol withdrawal syndrome			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Depression			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			

Hepatic enzyme increased				
subjects affected / exposed	0 / 538 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oxygen saturation decreased				
subjects affected / exposed	0 / 538 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Weight decreased				
subjects affected / exposed	0 / 538 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Alanine aminotransferase increased				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Aspartate aminotransferase increased				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Blood creatinine increased				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Blood pressure increased				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gamma-glutamyltransferase increased				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Neutrophil count decreased				

subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transaminases increased			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	2 / 538 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Thoracic vertebral fracture			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ankle fracture			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cervical vertebral fracture			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Craniocerebral injury			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femur fracture			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Foot fracture			

subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hip fracture			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Radiation skin injury			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rib fracture			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Spinal compression fracture			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Toxicity to various agents			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wrist fracture			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fall			

subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Head injury			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Radiation mucositis			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	4 / 538 (0.74%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	4 / 538 (0.74%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Sinus bradycardia			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute myocardial infarction			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Aortic valve incompetence			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Arrhythmia			

subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Atrial flutter				
subjects affected / exposed	2 / 538 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Atrioventricular block complete				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure acute				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Mitral valve incompetence				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial ischaemia				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	2 / 538 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Ventricular arrhythmia				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Ventricular extrasystoles				

subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ventricular tachycardia			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Angina unstable			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiopulmonary failure			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Haemorrhage intracranial			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Paraparesis			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Presyncope			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tremor			

subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Balance disorder			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebral haematoma			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebral haemorrhage			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebral ischaemia			
subjects affected / exposed	2 / 538 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Epilepsy			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ischaemic stroke			
subjects affected / exposed	3 / 538 (0.56%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			

subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	2 / 538 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Central nervous system lesion			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Muscle spasticity			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 538 (0.74%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	0 / 0		
Autoimmune haemolytic anaemia			
subjects affected / exposed	2 / 538 (0.37%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	40 / 538 (7.43%)		
occurrences causally related to treatment / all	34 / 46		
deaths causally related to treatment / all	1 / 1		
Haemolytic anaemia			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutropenia			

subjects affected / exposed	62 / 538 (11.52%)		
occurrences causally related to treatment / all	61 / 97		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	17 / 538 (3.16%)		
occurrences causally related to treatment / all	16 / 17		
deaths causally related to treatment / all	0 / 0		
Pancytopenia			
subjects affected / exposed	4 / 538 (0.74%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	0 / 0		
Leukopenia			
subjects affected / exposed	3 / 538 (0.56%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	0 / 0		
Lymphopenia			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bicytopenia			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Lower gastrointestinal haemorrhage				
subjects affected / exposed	0 / 538 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stomatitis				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal pain upper				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ascites				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Diverticular perforation				
subjects affected / exposed	2 / 538 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Haematochezia				

subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal perforation			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mouth haemorrhage			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peritoneal adhesions			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	2 / 538 (0.37%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutropenic colitis			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholangitis			

subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholecystitis			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic failure			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatocellular injury			
subjects affected / exposed	3 / 538 (0.56%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Acute hepatic failure			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Cholecystitis acute			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatitis			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatitis toxic			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Liver disorder			

subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Drug-induced liver injury			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dermatitis allergic			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Purpura			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Diabetic foot			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rash maculo-papular			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Drug eruption			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urticaria			

subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute kidney injury			
subjects affected / exposed	4 / 538 (0.74%)		
occurrences causally related to treatment / all	2 / 5		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	2 / 538 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hypertensive nephropathy			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal impairment			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urethral prolapse			

subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract obstruction			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Hypercalcaemia of malignancy			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperparathyroidism			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperthyroidism			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fistula inflammation			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Osteoarthritis			
subjects affected / exposed	4 / 538 (0.74%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Rheumatoid arthritis			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal column stenosis			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal pain			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Arthritis			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bacterial sepsis			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	2 / 538 (0.37%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Clostridium difficile colitis			

subjects affected / exposed	0 / 538 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterococcal sepsis				
subjects affected / exposed	0 / 538 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	2 / 538 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Fungal infection				
subjects affected / exposed	2 / 538 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Herpes simplex				
subjects affected / exposed	0 / 538 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	4 / 538 (0.74%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	4 / 538 (0.74%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 538 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				

subjects affected / exposed	2 / 538 (0.37%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Oropharyngeal candidiasis				
subjects affected / exposed	0 / 538 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	52 / 538 (9.67%)			
occurrences causally related to treatment / all	19 / 70			
deaths causally related to treatment / all	0 / 6			
Pneumonia viral				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Progressive multifocal leukoencephalopathy				
subjects affected / exposed	0 / 538 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	5 / 538 (0.93%)			
occurrences causally related to treatment / all	3 / 5			
deaths causally related to treatment / all	0 / 2			
Septic shock				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Sinusitis				
subjects affected / exposed	0 / 538 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Staphylococcal sepsis				

subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Subcutaneous abscess			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tracheobronchitis			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	6 / 538 (1.12%)		
occurrences causally related to treatment / all	1 / 6		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal sepsis			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Abscess limb			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute hepatitis B			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Arthritis infective			

subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Aspergillus infection				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Atypical pneumonia				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Brain abscess				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Bronchitis bacterial				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchopulmonary aspergillosis				
subjects affected / exposed	3 / 538 (0.56%)			
occurrences causally related to treatment / all	3 / 4			
deaths causally related to treatment / all	1 / 1			
Campylobacter gastroenteritis				
subjects affected / exposed	2 / 538 (0.37%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Campylobacter infection				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cellulitis				

subjects affected / exposed	3 / 538 (0.56%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Clostridium colitis				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile infection				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cryptosporidiosis infection				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cytomegalovirus infection				
subjects affected / exposed	4 / 538 (0.74%)			
occurrences causally related to treatment / all	1 / 5			
deaths causally related to treatment / all	0 / 0			
Device related infection				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	2 / 538 (0.37%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Ear infection				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Eczema infected				

subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Encephalitis viral				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Endocarditis				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia bacteraemia				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	2 / 538 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Giardiasis				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
H1N1 influenza				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Herpes zoster oticus				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infected skin ulcer				

subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatitis B				
subjects affected / exposed	2 / 538 (0.37%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Infective exacerbation chronic obstructive airways disease				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	4 / 538 (0.74%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			
Lymphangitis				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Meningitis				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Meningitis cryptococcal				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Myringitis bullous				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nasopharyngitis				

subjects affected / exposed	2 / 538 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Neutropenic sepsis			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Oral candidiasis			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Perirectal abscess			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia cytomegaloviral			
subjects affected / exposed	2 / 538 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumonia pseudomonal			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Pseudomembranous colitis			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pseudomonal sepsis			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pyelonephritis			

subjects affected / exposed	2 / 538 (0.37%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Splenic abscess				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Viral infection				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	2 / 538 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Visceral leishmaniasis				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
West nile viral infection				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Wound infection				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia infection				
subjects affected / exposed	0 / 538 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fungal oesophagitis				

subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebral toxoplasmosis			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Herpes virus infection			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Laryngitis viral			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Listeriosis			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peritonitis			
subjects affected / exposed	1 / 538 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumococcal sepsis			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia fungal			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia pneumococcal			

subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Retinitis viral			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Varicella zoster virus infection			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung infection pseudomonal			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia bacterial			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin infection			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection enterococcal			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Tumour lysis syndrome			

subjects affected / exposed	29 / 538 (5.39%)			
occurrences causally related to treatment / all	27 / 29			
deaths causally related to treatment / all	2 / 2			
Diabetes mellitus				
subjects affected / exposed	3 / 538 (0.56%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Diabetes mellitus inadequate control				
subjects affected / exposed	2 / 538 (0.37%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Hypercalcaemia				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperglycaemia				
subjects affected / exposed	2 / 538 (0.37%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Hyperuricaemia				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Malnutrition				
subjects affected / exposed	1 / 538 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Type 2 diabetes mellitus				
subjects affected / exposed	2 / 538 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Fluid overload				

subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	0 / 538 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	G-Mono	G-FC	G-Clb
Total subjects affected by non-serious adverse events			
subjects affected / exposed	102 / 126 (80.95%)	184 / 193 (95.34%)	106 / 114 (92.98%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 126 (3.17%)	11 / 193 (5.70%)	2 / 114 (1.75%)
occurrences (all)	4	12	2
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 126 (3.17%)	10 / 193 (5.18%)	5 / 114 (4.39%)
occurrences (all)	4	10	6
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 126 (3.97%)	16 / 193 (8.29%)	5 / 114 (4.39%)
occurrences (all)	5	16	5
Hypotension			
subjects affected / exposed	10 / 126 (7.94%)	17 / 193 (8.81%)	16 / 114 (14.04%)
occurrences (all)	12	20	19
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 126 (6.35%)	22 / 193 (11.40%)	10 / 114 (8.77%)
occurrences (all)	15	24	10
Tremor			
subjects affected / exposed	6 / 126 (4.76%)	2 / 193 (1.04%)	6 / 114 (5.26%)
occurrences (all)	6	2	6
Dizziness			

subjects affected / exposed occurrences (all)	2 / 126 (1.59%) 4	3 / 193 (1.55%) 3	8 / 114 (7.02%) 8
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	19 / 126 (15.08%)	50 / 193 (25.91%)	26 / 114 (22.81%)
occurrences (all)	26	74	33
Leukopenia			
subjects affected / exposed	5 / 126 (3.97%)	23 / 193 (11.92%)	8 / 114 (7.02%)
occurrences (all)	8	41	12
Neutropenia			
subjects affected / exposed	45 / 126 (35.71%)	136 / 193 (70.47%)	58 / 114 (50.88%)
occurrences (all)	130	409	121
Thrombocytopenia			
subjects affected / exposed	27 / 126 (21.43%)	66 / 193 (34.20%)	35 / 114 (30.70%)
occurrences (all)	34	113	52
Lymphopenia			
subjects affected / exposed	2 / 126 (1.59%)	11 / 193 (5.70%)	2 / 114 (1.75%)
occurrences (all)	2	19	3
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	6 / 126 (4.76%)	30 / 193 (15.54%)	13 / 114 (11.40%)
occurrences (all)	7	42	16
Chest discomfort			
subjects affected / exposed	7 / 126 (5.56%)	7 / 193 (3.63%)	3 / 114 (2.63%)
occurrences (all)	7	7	3
Chills			
subjects affected / exposed	17 / 126 (13.49%)	30 / 193 (15.54%)	17 / 114 (14.91%)
occurrences (all)	18	32	20
Fatigue			
subjects affected / exposed	7 / 126 (5.56%)	19 / 193 (9.84%)	22 / 114 (19.30%)
occurrences (all)	7	24	26
Pyrexia			
subjects affected / exposed	26 / 126 (20.63%)	58 / 193 (30.05%)	27 / 114 (23.68%)
occurrences (all)	30	90	38
Oedema peripheral			

subjects affected / exposed occurrences (all)	3 / 126 (2.38%) 4	3 / 193 (1.55%) 4	9 / 114 (7.89%) 15
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	6 / 126 (4.76%)	24 / 193 (12.44%)	14 / 114 (12.28%)
occurrences (all)	7	30	16
Diarrhoea			
subjects affected / exposed	6 / 126 (4.76%)	38 / 193 (19.69%)	10 / 114 (8.77%)
occurrences (all)	8	43	11
Nausea			
subjects affected / exposed	22 / 126 (17.46%)	76 / 193 (39.38%)	25 / 114 (21.93%)
occurrences (all)	26	148	32
Vomiting			
subjects affected / exposed	8 / 126 (6.35%)	44 / 193 (22.80%)	14 / 114 (12.28%)
occurrences (all)	8	67	15
Abdominal pain			
subjects affected / exposed	3 / 126 (2.38%)	10 / 193 (5.18%)	4 / 114 (3.51%)
occurrences (all)	5	10	5
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	15 / 126 (11.90%)	28 / 193 (14.51%)	15 / 114 (13.16%)
occurrences (all)	16	33	16
Dyspnoea			
subjects affected / exposed	9 / 126 (7.14%)	24 / 193 (12.44%)	11 / 114 (9.65%)
occurrences (all)	9	24	13
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	5 / 126 (3.97%)	8 / 193 (4.15%)	7 / 114 (6.14%)
occurrences (all)	5	8	7
Pruritus			
subjects affected / exposed	4 / 126 (3.17%)	10 / 193 (5.18%)	2 / 114 (1.75%)
occurrences (all)	4	10	2
Rash			
subjects affected / exposed	4 / 126 (3.17%)	24 / 193 (12.44%)	11 / 114 (9.65%)
occurrences (all)	4	31	15
Musculoskeletal and connective tissue disorders			

Arthralgia subjects affected / exposed occurrences (all)	7 / 126 (5.56%) 9	7 / 193 (3.63%) 8	8 / 114 (7.02%) 10
Back pain subjects affected / exposed occurrences (all)	6 / 126 (4.76%) 6	13 / 193 (6.74%) 14	10 / 114 (8.77%) 11
Infections and infestations			
Bronchitis subjects affected / exposed occurrences (all)	8 / 126 (6.35%) 8	15 / 193 (7.77%) 19	5 / 114 (4.39%) 6
Influenza subjects affected / exposed occurrences (all)	5 / 126 (3.97%) 5	11 / 193 (5.70%) 11	4 / 114 (3.51%) 4
Nasopharyngitis subjects affected / exposed occurrences (all)	8 / 126 (6.35%) 10	16 / 193 (8.29%) 19	3 / 114 (2.63%) 3
Upper respiratory tract infection subjects affected / exposed occurrences (all)	5 / 126 (3.97%) 6	12 / 193 (6.22%) 14	5 / 114 (4.39%) 8
Urinary tract infection subjects affected / exposed occurrences (all)	5 / 126 (3.97%) 8	6 / 193 (3.11%) 8	8 / 114 (7.02%) 13
Sinusitis subjects affected / exposed occurrences (all)	2 / 126 (1.59%) 2	13 / 193 (6.74%) 17	5 / 114 (4.39%) 7
Respiratory tract infection subjects affected / exposed occurrences (all)	4 / 126 (3.17%) 5	4 / 193 (2.07%) 5	6 / 114 (5.26%) 6
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	3 / 126 (2.38%) 3	11 / 193 (5.70%) 15	10 / 114 (8.77%) 11
Hyperuricaemia subjects affected / exposed occurrences (all)	0 / 126 (0.00%) 0	6 / 193 (3.11%) 7	10 / 114 (8.77%) 11

Non-serious adverse events	G-Benda		
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Total subjects affected by non-serious adverse events subjects affected / exposed	499 / 538 (92.75%)		
Investigations			
Alanine aminotransferase increased subjects affected / exposed	12 / 538 (2.23%)		
occurrences (all)	13		
Aspartate aminotransferase increased subjects affected / exposed	15 / 538 (2.79%)		
occurrences (all)	15		
Vascular disorders			
Hypertension subjects affected / exposed	44 / 538 (8.18%)		
occurrences (all)	52		
Hypotension subjects affected / exposed	53 / 538 (9.85%)		
occurrences (all)	61		
Nervous system disorders			
Headache subjects affected / exposed	44 / 538 (8.18%)		
occurrences (all)	55		
Tremor subjects affected / exposed	11 / 538 (2.04%)		
occurrences (all)	11		
Dizziness subjects affected / exposed	22 / 538 (4.09%)		
occurrences (all)	23		
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed	131 / 538 (24.35%)		
occurrences (all)	171		
Leukopenia subjects affected / exposed	69 / 538 (12.83%)		
occurrences (all)	117		
Neutropenia subjects affected / exposed	283 / 538 (52.60%)		
occurrences (all)	619		
Thrombocytopenia			

subjects affected / exposed	161 / 538 (29.93%)		
occurrences (all)	252		
Lymphopenia			
subjects affected / exposed	53 / 538 (9.85%)		
occurrences (all)	88		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	44 / 538 (8.18%)		
occurrences (all)	57		
Chest discomfort			
subjects affected / exposed	15 / 538 (2.79%)		
occurrences (all)	15		
Chills			
subjects affected / exposed	89 / 538 (16.54%)		
occurrences (all)	106		
Fatigue			
subjects affected / exposed	70 / 538 (13.01%)		
occurrences (all)	84		
Pyrexia			
subjects affected / exposed	172 / 538 (31.97%)		
occurrences (all)	244		
Oedema peripheral			
subjects affected / exposed	31 / 538 (5.76%)		
occurrences (all)	37		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	71 / 538 (13.20%)		
occurrences (all)	83		
Diarrhoea			
subjects affected / exposed	80 / 538 (14.87%)		
occurrences (all)	110		
Nausea			
subjects affected / exposed	145 / 538 (26.95%)		
occurrences (all)	207		
Vomiting			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>69 / 538 (12.83%)</p> <p>87</p>			
<p>Abdominal pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>23 / 538 (4.28%)</p> <p>29</p>			
<p>Respiratory, thoracic and mediastinal disorders</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>55 / 538 (10.22%)</p> <p>68</p> <p>Dyspnoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>53 / 538 (9.85%)</p> <p>67</p>			
<p>Skin and subcutaneous tissue disorders</p> <p>Hyperhidrosis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>20 / 538 (3.72%)</p> <p>21</p> <p>Pruritus</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>23 / 538 (4.28%)</p> <p>28</p> <p>Rash</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>44 / 538 (8.18%)</p> <p>60</p>			
<p>Musculoskeletal and connective tissue disorders</p> <p>Arthralgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>20 / 538 (3.72%)</p> <p>22</p> <p>Back pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>35 / 538 (6.51%)</p> <p>36</p>			
<p>Infections and infestations</p> <p>Bronchitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>35 / 538 (6.51%)</p> <p>38</p> <p>Influenza</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>11 / 538 (2.04%)</p> <p>14</p>			

Nasopharyngitis subjects affected / exposed occurrences (all)	23 / 538 (4.28%) 26		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	43 / 538 (7.99%) 52		
Urinary tract infection subjects affected / exposed occurrences (all)	26 / 538 (4.83%) 33		
Sinusitis subjects affected / exposed occurrences (all)	16 / 538 (2.97%) 18		
Respiratory tract infection subjects affected / exposed occurrences (all)	10 / 538 (1.86%) 15		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	43 / 538 (7.99%) 44		
Hyperuricaemia subjects affected / exposed occurrences (all)	32 / 538 (5.95%) 35		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 March 2013	<ol style="list-style-type: none">1. The original protocol was amended to reflect changes in the safety profile of obinutuzumab with regard to a higher incidence of thrombocytopenia and hemorrhagic events during the first cycle in subjects with CLL treated with obinutuzumab plus chlorambucil, as compared to subjects treated with rituximab plus chlorambucil or chlorambucil alone, in the Phase 3 pivotal study NCT010100612. Investigators were requested to closely monitor all subjects treated with obinutuzumab for thrombocytopenia and signs of hemorrhage, especially during the first cycle.
09 October 2014	<ol style="list-style-type: none">1. To ensure that subject safety was not put at risk by clarifying inconsistencies and thereby reducing protocol violations2. The amendment also included criteria for defining tumor lysis syndrome (TLS) and additional guidance regarding the risk of TLS, reinforcing adherence to the protocol when treating and monitoring subjects in the study.
06 May 2015	<ol style="list-style-type: none">1. Addition of an interim efficacy analysis in a subgroup of subjects in Cohort 1 treated with obinutuzumab plus bendamustine, amendment of the secondary endpoint regarding response assessment from "ORR at end of treatment" to "CR and ORR at the time of FRA visit" for clarity, addition of Cohort 3 design per recommendations of the study IDMC, and removal of short-duration infusion-related assessments2. Short-duration infusion was defined as the full 1000 mg obinutuzumab dose administered over 90 minutes, i.e., at a rate of approximately 667 mg/hour, rather than at the prior maximum rate of 400 mg/hour. The exploratory objective to examine the safety and PK profile of subjects who were to receive the short-duration infusion was removed.
27 October 2015	Addition of gastro-intestinal (GI) perforation as an important risk based on data from a trial in subjects with non Hodgkin's lymphoma (NHL) treated with obinutuzumab in combination with bendamustine.
06 March 2016	<ol style="list-style-type: none">1. To implement additional risk minimization measures in subjects with CLL at risk of TLS treated with a combination of obinutuzumab and bendamustine. This followed the occurrence of a second fatal case of TLS in a subject at risk of TLS treated for CLL with obinutuzumab and bendamustine. More detailed criteria, including renal impairment in addition to criteria relating to tumor load, were added to identify subjects in this treatment group considered to be at high risk of TLS. The risk minimization measures included additional monitoring and laboratory assessments during Cycle 1.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported