Clinical trial results:
A randomized, controlled, double-blind Phase III trial to compare the efficacy, safety and pharmacokinetics of GP2013 plus cyclophosphamide, vincristine, prednisone vs. MabThera® plus cyclophosphamide, vincristine, prednisone, followed by GP2013 or MabThera® maintenance therapy in patients with previously untreated, advanced stage follicular lymphoma

Summary

EudraCT number	2010-019522-13
Trial protocol	NL PT FR HU DE AT BG ES PL GR IT GB IE
Global end of trial date	22 January 2018

Results information

Result version number	v1 (current)
This version publication date	06 February 2019
First version publication date	06 February 2019

Trial information

Trial identification

Sponsor protocol code	CIGG013A2301J

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01419665
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hexal AG/ Novartis Pharmaceuticals
Sponsor organisation address	Industriestr. 25, Holzkirchen, Germany, D-83607
Public contact	Study Director, Hexal AG / Novartis, 41 613241111, novartis.email@novartis.com
Scientific contact	Study Director, Hexal AG / Novartis Pharmaceuticals, +41 613241111, novartis.email@novartis.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	22 January 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 January 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to demonstrate comparability of the overall response rate (ORR) in patients with previously untreated, advanced stage follicular lymphoma who received GP2013-CVP combination treatment to patients who received MabThera-CVP combination treatment.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy:

cyclophosphamide, vincristine, prednisone

Evidence for comparator:

MabThera

Actual start date of recruitment	01 December 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 27
Country: Number of subjects enrolled	Argentina: 5
Country: Number of subjects enrolled	Austria: 6
Country: Number of subjects enrolled	Bulgaria: 15
Country: Number of subjects enrolled	Brazil: 102
Country: Number of subjects enrolled	Colombia: 2
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Greece: 9
Country: Number of subjects enrolled	Hungary: 14
Country: Number of subjects enrolled	India: 94
Country: Number of subjects enrolled	Ireland: 2
Country: Number of subjects enrolled	Israel: 12
Country: Number of subjects enrolled	Italy: 23
Country: Number of subjects enrolled	Japan: 29

Country: Number of subjects enrolled	Malaysia: 30
Country: Number of subjects enrolled	Netherlands: 17
Country: Number of subjects enrolled	Peru: 9
Country: Number of subjects enrolled	Poland: 41
Country: Number of subjects enrolled	Portugal: 33
Country: Number of subjects enrolled	Romania: 13
Country: Number of subjects enrolled	Russian Federation: 46
Country: Number of subjects enrolled	South Africa: 28
Country: Number of subjects enrolled	Spain: 37
Country: Number of subjects enrolled	Ukraine: 21
Worldwide total number of subjects	627
EEA total number of subjects	222

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)	461
From 65 to 84 years	166
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 629 patients were randomized at 159 centers in 26 countries, 314 patients to GP2013 (312 patients treated) and 315 to MabThera. Of those 314 patients in the GP2013 group, 2 patients were randomized by error and discontinued before any treatment with GP2013. The number of patients in both treatment groups remained similar.

Pre-assignment

Screening details:

full analysis set participants :
GP2013 312 MabThera 315
safety set participants :
GP2013 312 MabThera 315
per protocol set participants: GP2013 310 MabThera 312
pharmacokinetic analysis set 1 : GP2013 119 MabThera 120
immunogenicity analysis set: GP2013 275 MabThera 287
pharmacodynamic analysis set : GP2013 24 MabThera 24

Period 1

Period 1 title	combination treatment
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Subject, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	GP2013

Arm description:

Experimental Type: Biological/Vaccine

Arm type	Experimental
Investigational medicinal product name	GP2013
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

GP2013 was provided as sterile, colorless, preservative-free liquid concentrate for solution for i.v. infusion. It was supplied at a
concentration of 10 mg/mL in 500 mg (50 mL) single use vials.

Arm title	MabThera

Arm description:

Comparator Type: Biological/Vaccine

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

Dosage and administration details:

MabThera (Roche Registration Ltd.) was provided as sterile, colorless, preservative-free liquid concentrate for solution for i.v. infusion. It was supplied at a concentration of 10 mg/mL in 500 mg (50 mL) single use vials.

Number of subjects in period 1	GP2013	MabThera
Started	312	315
Completed	274	274
Not completed	38	41
Adverse event, serious fatal	5	7
Physician decision	5	8
Consent withdrawn by subject	5	4
Adverse event, non-fatal	7	10
administrative problems	-	1
disease progression	10	9
Protocol deviation	6	2

Period 2	
Period 2 title	Maintenance treatment and/or follow up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms	
Are arms mutually exclusive?	Yes
Arm title	GP2013

Arm description:

Experimental Type: Biological/Vaccine

Arm type	Experimental
Investigational medicinal product name	GP2013
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

GP2013 was provided as sterile, colorless, preservative-free liquid concentrate for solution for i.v. infusion. It was supplied at a
concentration of 10 mg/mL in 500 mg (50 mL) single use vials.

Arm title	MabThera

Arm description:

Comparator Type: Biological/Vaccine

Arm type	Active comparator

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

Dosage and administration details:

MabThera (Roche Registration Ltd.) was provided as sterile, colorless, preservative-free liquid concentrate for solution for i.v. infusion. It was supplied at a concentration of 10 mg/mL in 500 mg (50 mL) single use vials.

Number of subjects in period 2[1]	GP2013	MabThera
Started	254	252
Completed	132	150
Not completed	122	102
Adverse event, serious fatal	1	2
Consent withdrawn by subject	6	6
Physician decision	5	2
Adverse event, non-fatal	11	7
switch to open label	44	39
administrative problems	-	6
Lost to follow-up	1	2
disease progression	53	37
Protocol deviation	1	1

Notes:

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

Period 3

Period 3 title	open label phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	MabThera

Arm description:

Experimental Type: Biological/Vaccine, all patients switched to MabThera

Arm type	all patients in this phase received MabThera

No investigational medicinal product assigned in this arm

Arm title	MabThera

Arm description:

Comparator Type: Biological/Vaccine

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

Dosage and administration details:

MabThera (Roche Registration Ltd.) was provided as sterile, colorless, preservative-free liquid concentrate for solution for i.v. infusion. It was supplied at a concentration of 10 mg/mL in 500 mg (50 mL) single use vials.

Number of subjects in period 3[2]	MabThera	MabThera
Started	44	39
Completed	43	38
Not completed	1	1
Adverse event, serious fatal	1	-
disease progression	-	1

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: numbers are correct

Baseline characteristics

Reporting groups	
Reporting group title	GP2013
Reporting group description:	
Experimental Type: Biological/Vaccine	
Reporting group title	MabThera
Reporting group description:	
Comparator Type: Biological/Vaccine	

Reporting group values	GP2013	MabThera	Total
Number of subjects	312	315	627
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	226	235	461
From 65-84 years	86	80	166
85 years and over	0	0	0
Age Continuous			
Units: years			
arithmetic mean	57.5	56.4	
standard deviation	± 11.86	± 11.72	-
Sex: Female, Male			
Units: Subjects			
Female	181	169	350
Male	131	146	277
Race, Customized			
Race			
Units: Subjects			
Asian	71	85	156
Black	6	3	9
Caucasian	214	207	421
Native American	2	5	7
Other	19	15	34
Ethnicity, Customized			
Ethnicity			
Units: Subjects			
Chinese	5	6	11
Hispanic / Latino	59	68	127
Indian (Indian Subcontinent)	40	54	94
Mixed Ethnicity	8	3	11
Other	183	170	353

Unknown / missing	1	0	1
Japanese	16	14	30

End points

End points reporting groups	
Reporting group title	GP2013
Reporting group description: Experimental Type: Biological/Vaccine	
Reporting group title	MabThera
Reporting group description: Comparator Type: Biological/Vaccine	
Reporting group title	GP2013
Reporting group description: Experimental Type: Biological/Vaccine	
Reporting group title	MabThera
Reporting group description: Comparator Type: Biological/Vaccine	
Reporting group title	MabThera
Reporting group description: Experimental Type: Biological/Vaccine, all patients switched to MabThera	
Reporting group title	MabThera
Reporting group description: Comparator Type: Biological/Vaccine	

Primary: Overall response rate (ORR)	
End point title	Overall response rate (ORR)
End point description: ORR is defined as the proportion of patients whose best overall disease response was either CR or PR during the combination treatment period based on blinded independent central radiology review. Per protocol set.	
End point type	Primary
End point timeframe: 24 weeks	

End point values	GP2013	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	311	313		
Units: percentage				
number (confidence interval 90%)	87.1 (83.59 to 90.15)	87.5 (84.04 to 90.49)		

Statistical analyses

Statistical analysis title	comparison of ORR between the 2 arms
Statistical analysis description: Equivalence to be concluded if the entire 95% CI of the difference in ORR between both groups is within	

the pre-specified margin of (-12%, 12%).

Comparison groups	GP2013 v MabThera
Number of subjects included in analysis	624
Analysis specification	Pre-specified
Analysis type	equivalence[1]
Method	Binomial approximation
Parameter estimate	difference in ORR (GP2013 –MabThera)
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.94
upper limit	5.14

Notes:

[1] - The equivalence margin of + or - 12% was determined considering the variability of the point estimate of the add-on effect by taking a value lower than the lower boundary of the 95% CI for Rituximab+chemotherapy versus chemotherapy obtained from historical data.

Secondary: To evaluate the Complete Response (CR) rate during the combination treatment period

End point title	To evaluate the Complete Response (CR) rate during the combination treatment period
End point description:	
Per protocol set	
End point type	Secondary
End point timeframe:	
24 weeks	

End point values	GP2013	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	311	313		
Units: participants	46	42		

Statistical analyses

No statistical analyses for this end point

Secondary: To evaluate the Partial Response (PR) rate during the combination treatment period

End point title	To evaluate the Partial Response (PR) rate during the combination treatment period
End point description:	
Per protocol set	
End point type	Secondary
End point timeframe:	
24 weeks	

End point values	GP2013	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	311	313		
Units: participants	225	232		

Statistical analyses

No statistical analyses for this end point

Secondary: To evaluate the progression free survival (PFS) with up to 3 years of follow-up post randomization

End point title	To evaluate the progression free survival (PFS) with up to 3 years of follow-up post randomization

End point description:

Number of participants with progression free survival events. PFS was defined as the time from the date of randomization to the date of event defined as the first observation of documented disease progression or death due to any cause.
full analysis set

End point type	Secondary

End point timeframe:

3 years

End point values	GP2013	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	312	315		
Units: participants	97	78		

Statistical analyses

Statistical analysis title	PFS

Statistical analysis description:

PFS evaluation was based on the investigators' assessment of documented disease Progression.

If a patient did not have an event, PFS was censored at the date of last adequate Tumor assessment. The PFS analysis contained data from the Combination Phase, the Maintenance Phase, the Open-label Phase, and the Follow-up Phase of the study.

Comparison groups	GP2013 v MabThera

Number of subjects included in analysis	627
Analysis specification	Pre-specified
Analysis type	
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	1.76

Secondary: Overall survival (OS) with up to 3 years of follow- up post randomization, as assessed by the number of deaths

End point title	Overall survival (OS) with up to 3 years of follow- up post randomization, as assessed by the number of deaths

End point description:

OS was defined as the time from date of randomization to date of death due to any cause. If a patient was not known to have died, OS was censored at the date of last contact.
full analysis set

End point type	Secondary

End point timeframe:

3 years

End point values	GP2013	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	312	315		
Units: participants	29	31		

Statistical analyses

Statistical analysis title	Overall Survival
Comparison groups	GP2013 v MabThera
Number of subjects included in analysis	627
Analysis specification	Pre-specified
Analysis type	
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.52

Secondary: To evaluate the incidence of immunogenicity (ADA formation) against GP2013 and MabThera (rituximab)

End point title	To evaluate the incidence of immunogenicity (ADA formation) against GP2013 and MabThera (rituximab)

End point description:

number of participants with confirmed positive ADA
immunogenicity analysis set

End point type	Secondary

End point timeframe:

24 weeks, 3 years

End point values	GP2013	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	287		
Units: participants				
end of treatment combination phase (24 weeks)	1	2		
end of treatment manintenance phase (3 years)	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: To evaluate a PK marker following the treatment with GP2013-Chemotherapy and MabThera-Chemotherapy (Cmax)

End point title	To evaluate a PK marker following the treatment with GP2013-Chemotherapy and MabThera-Chemotherapy (Cmax)

End point description:

Cmax
PK analysis set 1

Day 63 is the C4D1 (cycle 4 day 1) of the combination phase

For descriptive purposes only, no hypothesis testing

End point type	Secondary

End point timeframe:

day 63

End point values	GP2013	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119[2]	120[3]		
Units: microg/mL				
geometric mean (geometric coefficient of variation)	333.59 (± 41.09)	331.93 (± 35.32)		

Notes:

[2] - number of participants with data : 108

[3] - number of participants with data : 111

Statistical analyses

No statistical analyses for this end point

Secondary: To evaluate a PK marker following the treatment with GP2013-Chemotherapy and MabThera-Chemotherapy (Ctrough)

End point title	To evaluate a PK marker following the treatment with GP2013-Chemotherapy and MabThera-Chemotherapy (Ctrough)

End point description:

Cthrough
PK analysis set 1
For descriptive purposes only, no hypothesis testing

End point type	Secondary

End point timeframe:

day 63

End point values	GP2013	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119[4]	120[5]		
Units: microg/mL				
arithmetic mean (standard deviation)	66.42 (± 47.593)	82.13 (± 61.526)		

Notes:

[4] - number of participants with data : 104

[5] - number of participants with data : 110

Statistical analyses

No statistical analyses for this end point

Secondary: To evaluate a PD marker (peripheral CD19+ B-cell counts) following the treatment with GP2013 + Chemotherapy and MabThera- Chemotherapy

End point title	To evaluate a PD marker (peripheral CD19+ B-cell counts) following the treatment with GP2013 + Chemotherapy and MabThera- Chemotherapy

End point description:

AUEC (0-21d)
PD analysis set
For descriptive purposes only, no hypothesis testing

End point type	Secondary

End point timeframe:

21 days

End point values	GP2013	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24[6]	24[7]		
Units: %*day				
geometric mean (geometric coefficient of variation)	1790 (± 23.5)	1910 (± 13.3)		

Notes:

[6] - number of participants with data : 19

[7] - number of participants with data : 18

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information
Timeframe for reporting adverse events:
Timeframe for AE
Adverse event reporting additional description:
AE additional description : Note that maintenance treatment phase data include the open label phase

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Combination GP2013+CVP
Reporting group description: Combination GP2013+CVP	
Reporting group title	Combination MabThera+CVP
Reporting group description: Combination MabThera+CVP	
Reporting group title	Maintenance GP2013
Reporting group description: Maintenance GP2013	
Reporting group title	Maintenance MabThera
Reporting group description: Maintenance MabThera	

Serious adverse events	Combination GP2013+CVP	Combination MabThera+CVP	Maintenance GP2013
Total subjects affected by serious adverse events			
subjects affected / exposed	71 / 312 (22.76%)	63 / 315 (20.00%)	24 / 254 (9.45%)
number of deaths (all causes)	4	5	2
number of deaths resulting from adverse events	3	2	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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

Lung neoplasm malignant			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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
Deep vein thrombosis			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Hypotension			
subjects affected / exposed	1 / 312 (0.32%)	1 / 315 (0.32%)	0 / 254 (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
Peripheral artery stenosis			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chills			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Fatigue			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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

Hypothermia			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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	0 / 312 (0.00%)	2 / 315 (0.63%)	0 / 254 (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
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 312 (0.32%)	1 / 315 (0.32%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	1 / 1	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Oedema peripheral			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Pain			
subjects affected / exposed	1 / 312 (0.32%)	1 / 315 (0.32%)	0 / 254 (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
Pyrexia			
subjects affected / exposed	4 / 312 (1.28%)	7 / 315 (2.22%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	1 / 4	2 / 8	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Immune system disorders			

Anaphylactic reaction			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Cytokine release syndrome			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Drug hypersensitivity			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Hypersensitivity			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Prostatism			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Scrotal swelling			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Uterine haemorrhage			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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

Vaginal haemorrhage			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Acute respiratory failure			
subjects affected / exposed	1 / 312 (0.32%)	1 / 315 (0.32%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Asthma			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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
Asthmatic crisis			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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 chronic			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Cough			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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

Dyspnoea			
subjects affected / exposed	0 / 312 (0.00%)	6 / 315 (1.90%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	1 / 312 (0.32%)	1 / 315 (0.32%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal pain			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Non-cardiogenic pulmonary oedema			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Pleural effusion			
subjects affected / exposed	0 / 312 (0.00%)	3 / 315 (0.95%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	1 / 254 (0.39%)
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 arterial hypertension			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Pulmonary embolism			
subjects affected / exposed	1 / 312 (0.32%)	3 / 315 (0.95%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pulmonary mass			

subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Pulmonary oedema			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 312 (0.32%)	1 / 315 (0.32%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Delirium			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Depression			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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
Mental disorder			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Suicide attempt			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Coagulation test abnormal			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Lipase increased			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Weight decreased			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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
Humerus fracture			

subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Infusion related reaction			
subjects affected / exposed	3 / 312 (0.96%)	1 / 315 (0.32%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	3 / 3	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple fractures			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Patella fracture			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Procedural pain			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Pubis fracture			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Upper limb fracture			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Congenital cystic kidney disease			

subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Hydrocele			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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
Polycystic liver disease			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Angina pectoris			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Atrial fibrillation			
subjects affected / exposed	1 / 312 (0.32%)	1 / 315 (0.32%)	0 / 254 (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
Atrial flutter			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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 arrest			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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			

subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Cardio-respiratory arrest			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Extrasystoles			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Palpitations			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Prinzmetal angina			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Tachycardia			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical cord compression			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Dementia			

subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Headache			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Ischaemic stroke			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	2 / 254 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Meningeal disorder			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Occipital neuralgia			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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 sensory neuropathy			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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
Syncope			

subjects affected / exposed	2 / 312 (0.64%)	0 / 315 (0.00%)	0 / 254 (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
Vascular dementia			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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 and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 312 (0.00%)	2 / 315 (0.63%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	15 / 312 (4.81%)	9 / 315 (2.86%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	14 / 17	12 / 13	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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
Leukopenia			
subjects affected / exposed	2 / 312 (0.64%)	2 / 315 (0.63%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Microcytic anaemia			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Neutropenia			

subjects affected / exposed	4 / 312 (1.28%)	5 / 315 (1.59%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	2 / 4	5 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Thrombocytopenia			
subjects affected / exposed	2 / 312 (0.64%)	0 / 315 (0.00%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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	4 / 312 (1.28%)	6 / 315 (1.90%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	1 / 4	2 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain lower			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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 upper			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Acute abdomen			

subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Ascites			
subjects affected / exposed	1 / 312 (0.32%)	1 / 315 (0.32%)	0 / 254 (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
Colitis			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Colitis microscopic			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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
Constipation			
subjects affected / exposed	3 / 312 (0.96%)	0 / 315 (0.00%)	0 / 254 (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
Diarrhoea			
subjects affected / exposed	1 / 312 (0.32%)	3 / 315 (0.95%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	1 / 1	1 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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
Erosive duodenitis			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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
Gastritis			

subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Gastrointestinal hypomotility			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus paralytic			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Intestinal obstruction			
subjects affected / exposed	0 / 312 (0.00%)	3 / 315 (0.95%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mouth ulceration			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Nausea			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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
Pancreatitis acute			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Small intestinal obstruction			

subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Vomiting			
subjects affected / exposed	0 / 312 (0.00%)	2 / 315 (0.63%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 312 (0.32%)	2 / 315 (0.63%)	0 / 254 (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
Hepatic cirrhosis			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Hepatic failure			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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 and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Toxic skin eruption			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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

Anuria			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Haematuria			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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
Hydronephrosis			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	2 / 254 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oliguria			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Pollakiuria			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Renal colic			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Renal failure			
subjects affected / exposed	2 / 312 (0.64%)	0 / 315 (0.00%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	3 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			

subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Endocrine disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 312 (0.00%)	2 / 315 (0.63%)	0 / 254 (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
Flank pain			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc disorder			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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 osteoarthritis			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Infections and infestations			
Abscess limb			

subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Anal abscess			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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
Appendicitis			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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			
subjects affected / exposed	2 / 312 (0.64%)	1 / 315 (0.32%)	0 / 254 (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
Cholecystitis infective			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Cystitis			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Diverticulitis			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometritis			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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
Erysipelas			

subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Escherichia infection			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Escherichia sepsis			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Gastroenteritis			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Gastroenteritis viral			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Genital herpes			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Helicobacter infection			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Hepatitis B			

subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	1 / 312 (0.32%)	1 / 315 (0.32%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious pleural effusion			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Influenza			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Malaria			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Oral candidiasis			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Peritonitis			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Peritonsillar abscess			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	0 / 254 (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			

subjects affected / exposed	3 / 312 (0.96%)	4 / 315 (1.27%)	3 / 254 (1.18%)
occurrences causally related to treatment / all	3 / 4	3 / 5	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumonia pseudomonal			
subjects affected / exposed	0 / 312 (0.00%)	0 / 315 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Respiratory tract infection			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	2 / 254 (0.79%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	2 / 312 (0.64%)	5 / 315 (1.59%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 2	2 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	3 / 312 (0.96%)	1 / 315 (0.32%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	2 / 3	1 / 1	0 / 1
deaths causally related to treatment / all	2 / 2	1 / 1	0 / 0
Tooth infection			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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 infection			

subjects affected / exposed	3 / 312 (0.96%)	1 / 315 (0.32%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Hyperglycaemia			
subjects affected / exposed	1 / 312 (0.32%)	1 / 315 (0.32%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Hyperuricaemia			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Hypervolaemia			
subjects affected / exposed	0 / 312 (0.00%)	1 / 315 (0.32%)	0 / 254 (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
Hypocalcaemia			

subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Hypoglycaemia			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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
Hyponatraemia			
subjects affected / exposed	2 / 312 (0.64%)	1 / 315 (0.32%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic acidosis			
subjects affected / exposed	1 / 312 (0.32%)	0 / 315 (0.00%)	0 / 254 (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

Serious adverse events	Maintenance MabThera		
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 252 (8.33%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung neoplasm malignant			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Vascular disorders			
Circulatory collapse			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peripheral artery stenosis			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chills			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypothermia			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Malaise				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Multiple organ dysfunction syndrome				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Non-cardiac chest pain				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oedema peripheral				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sudden death				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Anaphylactic reaction				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cytokine release syndrome				

subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Drug hypersensitivity				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypersensitivity				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Endometrial hyperplasia				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prostatism				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Scrotal swelling				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Uterine haemorrhage				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vaginal haemorrhage				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				

Acute pulmonary oedema			
subjects affected / exposed	0 / 252 (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 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute respiratory failure			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Asthma			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Asthmatic crisis			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchitis chronic			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cough			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Interstitial lung disease			

subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Laryngeal pain				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Non-cardiogenic pulmonary oedema				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary arterial hypertension				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary mass				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary oedema				

subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Confusional state				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Delirium				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depression				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mental disorder				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suicide attempt				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine aminotransferase increased				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aspartate aminotransferase				

increased				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coagulation test abnormal				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gamma-glutamyltransferase increased				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lipase increased				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Weight decreased				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Head injury				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Humerus fracture				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infusion related reaction				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Multiple fractures				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Patella fracture				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Procedural pain				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pubis fracture				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Toxicity to various agents				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper limb fracture				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Congenital, familial and genetic disorders				
Congenital cystic kidney disease				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hydrocele				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Polycystic liver disease			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Angina pectoris			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial flutter			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac failure			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardio-respiratory arrest			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Extrasystoles			

subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Palpitations				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prinzmetal angina				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tachycardia				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Cerebrovascular accident				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cervical cord compression				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dementia				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Headache				

subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hemiparesis				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningeal disorder				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Occipital neuralgia				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral sensory neuropathy				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular dementia				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				

subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	2 / 252 (0.79%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Leukocytosis				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Leukopenia				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lymphadenopathy				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Microcytic anaemia				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancytopenia				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				

subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Cataract			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain lower			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain upper			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute abdomen			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ascites			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colitis			

subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis microscopic				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Erosive duodenitis				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal hypomotility				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhoidal haemorrhage				

subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ileus paralytic				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mouth ulceration				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholelithiasis				

subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic cirrhosis				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic failure				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Skin and subcutaneous tissue disorders				
Drug eruption				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Toxic skin eruption				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Acute kidney injury				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Anuria				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematuria				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hydronephrosis				

subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephrolithiasis				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oliguria				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pollakiuria				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal colic				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal impairment				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Inappropriate antidiuretic hormone secretion				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				

Back pain				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Flank pain				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc disorder				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal osteoarthritis				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal pain				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abscess limb				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal abscess				
subjects affected / exposed	2 / 252 (0.79%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchitis				

subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis infective				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cystitis				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Endometritis				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia bacteraemia				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia infection				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia sepsis				

subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis viral			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Genital herpes			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Helicobacter infection			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatitis B			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Herpes zoster			
subjects affected / exposed	1 / 252 (0.40%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infectious pleural effusion			
subjects affected / exposed	0 / 252 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Influenza			

subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malaria				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oral candidiasis				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peritonsillar abscess				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia pseudomonal				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	1 / 252 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				

subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tooth infection				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	2 / 252 (0.79%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Viral infection				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Decreased appetite				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetes mellitus inadequate control				

subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperglycaemia				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperkalaemia				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperuricaemia				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypervolaemia				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypocalcaemia				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoglycaemia				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyponatraemia				
subjects affected / exposed	0 / 252 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolic acidosis				

subjects affected / exposed	0 / 252 (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	Combination GP2013+CVP	Combination MabThera+CVP	Maintenance GP2013
Total subjects affected by non-serious adverse events			
subjects affected / exposed	262 / 312 (83.97%)	255 / 315 (80.95%)	141 / 254 (55.51%)
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	41 / 312 (13.14%)	37 / 315 (11.75%)	5 / 254 (1.97%)
occurrences (all)	73	61	9
Vascular disorders			
Hypertension			
subjects affected / exposed	22 / 312 (7.05%)	15 / 315 (4.76%)	12 / 254 (4.72%)
occurrences (all)	28	17	15
Nervous system disorders			
Dizziness			
subjects affected / exposed	18 / 312 (5.77%)	12 / 315 (3.81%)	5 / 254 (1.97%)
occurrences (all)	19	12	6
Headache			
subjects affected / exposed	29 / 312 (9.29%)	34 / 315 (10.79%)	12 / 254 (4.72%)
occurrences (all)	45	51	19
Neuropathy peripheral			
subjects affected / exposed	49 / 312 (15.71%)	30 / 315 (9.52%)	8 / 254 (3.15%)
occurrences (all)	78	43	8
Paraesthesia			
subjects affected / exposed	24 / 312 (7.69%)	44 / 315 (13.97%)	7 / 254 (2.76%)
occurrences (all)	33	61	7
Peripheral sensory neuropathy			
subjects affected / exposed	26 / 312 (8.33%)	23 / 315 (7.30%)	6 / 254 (2.36%)
occurrences (all)	39	33	7
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	25 / 312 (8.01%)	28 / 315 (8.89%)	2 / 254 (0.79%)
occurrences (all)	55	58	2
Leukopenia			
subjects affected / exposed	23 / 312 (7.37%)	25 / 315 (7.94%)	11 / 254 (4.33%)
occurrences (all)	56	57	15
Neutropenia			
subjects affected / exposed	78 / 312 (25.00%)	91 / 315 (28.89%)	32 / 254 (12.60%)
occurrences (all)	177	220	41
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	30 / 312 (9.62%)	31 / 315 (9.84%)	12 / 254 (4.72%)
occurrences (all)	40	46	14
Fatigue			
subjects affected / exposed	35 / 312 (11.22%)	31 / 315 (9.84%)	6 / 254 (2.36%)
occurrences (all)	59	41	6
Oedema peripheral			
subjects affected / exposed	13 / 312 (4.17%)	24 / 315 (7.62%)	4 / 254 (1.57%)
occurrences (all)	13	37	4
Pyrexia			
subjects affected / exposed	27 / 312 (8.65%)	32 / 315 (10.16%)	12 / 254 (4.72%)
occurrences (all)	38	44	15
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	28 / 312 (8.97%)	35 / 315 (11.11%)	6 / 254 (2.36%)
occurrences (all)	35	46	6
Abdominal pain upper			
subjects affected / exposed	20 / 312 (6.41%)	16 / 315 (5.08%)	4 / 254 (1.57%)
occurrences (all)	24	17	4
Constipation			
subjects affected / exposed	69 / 312 (22.12%)	64 / 315 (20.32%)	8 / 254 (3.15%)
occurrences (all)	95	98	8
Diarrhoea			
subjects affected / exposed	39 / 312 (12.50%)	33 / 315 (10.48%)	11 / 254 (4.33%)
occurrences (all)	55	48	14
Nausea			

subjects affected / exposed	51 / 312 (16.35%)	42 / 315 (13.33%)	11 / 254 (4.33%)
occurrences (all)	77	66	11
Vomiting			
subjects affected / exposed	22 / 312 (7.05%)	26 / 315 (8.25%)	6 / 254 (2.36%)
occurrences (all)	34	38	9
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	32 / 312 (10.26%)	37 / 315 (11.75%)	33 / 254 (12.99%)
occurrences (all)	40	44	38
Dyspnoea			
subjects affected / exposed	16 / 312 (5.13%)	17 / 315 (5.40%)	5 / 254 (1.97%)
occurrences (all)	18	24	5
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	31 / 312 (9.94%)	26 / 315 (8.25%)	1 / 254 (0.39%)
occurrences (all)	34	27	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	15 / 312 (4.81%)	19 / 315 (6.03%)	3 / 254 (1.18%)
occurrences (all)	17	22	5
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	19 / 312 (6.09%)	21 / 315 (6.67%)	9 / 254 (3.54%)
occurrences (all)	20	27	11
Back pain			
subjects affected / exposed	26 / 312 (8.33%)	30 / 315 (9.52%)	14 / 254 (5.51%)
occurrences (all)	30	45	17
Myalgia			
subjects affected / exposed	17 / 312 (5.45%)	20 / 315 (6.35%)	4 / 254 (1.57%)
occurrences (all)	22	27	4
Pain in extremity			
subjects affected / exposed	19 / 312 (6.09%)	24 / 315 (7.62%)	7 / 254 (2.76%)
occurrences (all)	22	31	10
Infections and infestations			
Influenza			

subjects affected / exposed	16 / 312 (5.13%)	7 / 315 (2.22%)	7 / 254 (2.76%)
occurrences (all)	17	8	9
Upper respiratory tract infection			
subjects affected / exposed	22 / 312 (7.05%)	22 / 315 (6.98%)	12 / 254 (4.72%)
occurrences (all)	25	35	15
Urinary tract infection			
subjects affected / exposed	27 / 312 (8.65%)	22 / 315 (6.98%)	14 / 254 (5.51%)
occurrences (all)	34	33	19
Viral upper respiratory tract infection			
subjects affected / exposed	8 / 312 (2.56%)	10 / 315 (3.17%)	5 / 254 (1.97%)
occurrences (all)	9	10	7
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	17 / 312 (5.45%)	21 / 315 (6.67%)	3 / 254 (1.18%)
occurrences (all)	20	25	3
Hyperglycaemia			
subjects affected / exposed	17 / 312 (5.45%)	22 / 315 (6.98%)	4 / 254 (1.57%)
occurrences (all)	28	48	4
Hyperuricaemia			
subjects affected / exposed	8 / 312 (2.56%)	18 / 315 (5.71%)	5 / 254 (1.97%)
occurrences (all)	9	22	5

Non-serious adverse events	Maintenance MabThera		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	144 / 252 (57.14%)		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	4 / 252 (1.59%)		
occurrences (all)	11		
Vascular disorders			
Hypertension			
subjects affected / exposed	12 / 252 (4.76%)		
occurrences (all)	13		
Nervous system disorders			
Dizziness			

subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Neuropathy peripheral subjects affected / exposed occurrences (all) Paraesthesia subjects affected / exposed occurrences (all) Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	2 / 252 (0.79%) 2 14 / 252 (5.56%) 18 2 / 252 (0.79%) 3 4 / 252 (1.59%) 5 5 / 252 (1.98%) 7		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Leukopenia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all)	 5 / 252 (1.98%) 5 5 / 252 (1.98%) 9 16 / 252 (6.35%) 21		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all) Pyrexia	 11 / 252 (4.37%) 11 10 / 252 (3.97%) 12 11 / 252 (4.37%) 13		

subjects affected / exposed occurrences (all)	13 / 252 (5.16%) 15		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 7 / 252 (2.78%) 9 7 / 252 (2.78%) 9 10 / 252 (3.97%) 13 18 / 252 (7.14%) 19 8 / 252 (3.17%) 8 12 / 252 (4.76%) 12		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all)	 23 / 252 (9.13%) 28 4 / 252 (1.59%) 4		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	 1 / 252 (0.40%) 1		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	 4 / 252 (1.59%) 4		

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	21 / 252 (8.33%)		
occurrences (all)	26		
Back pain			
subjects affected / exposed	14 / 252 (5.56%)		
occurrences (all)	20		
Myalgia			
subjects affected / exposed	3 / 252 (1.19%)		
occurrences (all)	4		
Pain in extremity			
subjects affected / exposed	14 / 252 (5.56%)		
occurrences (all)	19		
Infections and infestations			
Influenza			
subjects affected / exposed	8 / 252 (3.17%)		
occurrences (all)	11		
Upper respiratory tract infection			
subjects affected / exposed	17 / 252 (6.75%)		
occurrences (all)	29		
Urinary tract infection			
subjects affected / exposed	25 / 252 (9.92%)		
occurrences (all)	35		
Viral upper respiratory tract infection			
subjects affected / exposed	15 / 252 (5.95%)		
occurrences (all)	28		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 252 (1.59%)		
occurrences (all)	4		
Hyperglycaemia			
subjects affected / exposed	9 / 252 (3.57%)		
occurrences (all)	11		
Hyperuricaemia			
subjects affected / exposed	10 / 252 (3.97%)		
occurrences (all)	14		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 February 2012	The key purpose of this protocol amendment was to update and clearly define the attributes of the study inclusion and exclusion criteria, revise the recommended dose modification per current clinical practice, and change the primary ORR analysis from local to central blinded review of radiological response.
21 January 2013	The primary purpose of this amendment was to allow lymph node biopsy samples collected within 5 months of screening to establish and confirm the diagnosis of follicular lymphoma. As follicular lymphoma is a slowly progressing disease and lymph node biopsy is considered an invasive procedure, lymph node biopsy samples collected within 5 months of screening were allowed to confirm patient eligibility. To simplify the assessment and interpretation of tuberculosis testing at Screening, the status of active tuberculosis infection was assessed as per the local standard of care for patient eligibility. Furthermore, the population PK of GP2013 and MabThera was removed in the amendment as this analysis was not deemed necessary to compare the PK of GP2013 and MabThera.
26 September 2013	The primary reason for this protocol amendment was to add a planned interim analysis (based on specific health authority feedback) to support the regulatory filing of GP2013 with EMA and potentially other health authorities.
10 November 2014	this amendment was based on health authority feedback received in Feb-2014, which led to the removal of the planned interim analysis added in protocol amendment version 4.0.
09 June 2016	The amendment text clarified that blinded monitors, medical monitors, data management, investigator site staff, and patients would be kept blinded (with the exception of the coordinating investigator who has to sign the CSR for the Combination Phase) until the final DBL.
23 February 2017	This amendment described a Urgent Safety Measure that was issued on 22-Dec-2016. The clinical batch of GP2013 was quarantined due to out-of-specification findings in routine stability testing.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported