Clinical trial results:
Protocol I4T-MC-JVCZ Randomized Phase 2 Trial Evaluating Alternative Ramucirumab Doses in Combination with Paclitaxel in Second-Line Metastatic or Locally Advanced, Unresectable Gastric or Gastroesophageal Junction Adenocarcinoma

Summary

EudraCT number	2014-005067-32
Trial protocol	DE CZ SE GR BE ES
Global end of trial date	28 December 2018

Results information

Result version number	v1 (current)
This version publication date	05 January 2020
First version publication date	05 January 2020

Trial information

Trial identification

Sponsor protocol code	I4T-MC-JVCZ

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02514551
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 15541

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559,

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	28 December 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 December 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study is to evaluate the efficacy of an alternative dose of ramucirumab in combination with paclitaxel in participants with second-line metastatic or locally advanced, unresectable gastric or gastroesophageal junction adenocarcinoma (GEJ).

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 October 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	21 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Greece: 21
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	Turkey: 40
Country: Number of subjects enrolled	Belgium: 11
Country: Number of subjects enrolled	United States: 24
Country: Number of subjects enrolled	Ukraine: 44
Country: Number of subjects enrolled	Italy: 23
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Spain: 56
Country: Number of subjects enrolled	Czech Republic: 16
Worldwide total number of subjects	245
EEA total number of subjects	133

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)	165
From 65 to 84 years	80
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

No Text Available

Pre-assignment

Screening details:

Completers are defined as participants who died or had progressive disease (PD) or completed treatment or did not complete treatment and were followed for survival data. Final study data will be provided after study completion.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	12mg/kg Ramucirumab + 80 mg/m² Paclitaxel

Arm description:

12 milligram per kilogram (mg/kg) ramucirumab administered intravenously (IV) on day 1 and day 15 (28 day cycles) in combination with 80 milligram per square meter (mg/m²) paclitaxel administered IV on day 1, day 8 and day 15.

Arm type	Experimental
Investigational medicinal product name	Ramucirumab
Investigational medicinal product code	
Other name	LY3009806,IMC-1121B,Cyramza
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

12 milligram per kilogram (mg/kg) ramucirumab administered intravenously (IV) on day 1 and day 15 (28 day cycles)

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

80 milligram per square meter (mg/m²) paclitaxel administered IV on day 1, day 8 and day 15.

Arm title	8 mg/kg Ramucirumab + 80 mg/m² Paclitaxel

Arm description:

8 mg/kg ramucirumab administered IV on day 1 and day 15 (28 day cycles) in combination with 80 mg/m² paclitaxel administered IV on day 1, day 8 and day 15.

Arm type	Active comparator
Investigational medicinal product name	Ramucirumab
Investigational medicinal product code	
Other name	LY3009806, IMC-1121B
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

8 mg/kg ramucirumab administered IV on day 1 and day 15 (28 day cycles).

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

80 mg/m² paclitaxel administered IV on day 1, day 8 and day 15.

Number of subjects in period 1	12mg/kg Ramucirumab + 80 mg/m² Paclitaxel	8 mg/kg Ramucirumab + 80 mg/m² Paclitaxel
Started	123	122
Received at least one dose of study drug	123	120
Completed	123	119
Not completed	0	3
Participant Never Treated	-	2
Lost to follow-up	-	1

Baseline characteristics

Reporting groups	
Reporting group title	12mg/kg Ramucirumab + 80 mg/m² Paclitaxel
Reporting group description:	
12 milligram per kilogram (mg/kg) ramucirumab administered intravenously (IV) on day 1 and day 15 (28 day cycles) in combination with 80 milligram per square meter (mg/m²) paclitaxel administered IV on day 1, day 8 and day 15.	
Reporting group title	8 mg/kg Ramucirumab + 80 mg/m² Paclitaxel
Reporting group description:	
8 mg/kg ramucirumab administered IV on day 1 and day 15 (28 day cycles) in combination with 80 mg/m² paclitaxel administered IV on day 1, day 8 and day 15.	

Reporting group values	12mg/kg Ramucirumab + 80 mg/m² Paclitaxel	8 mg/kg Ramucirumab + 80 mg/m² Paclitaxel	Total
Number of subjects	123	122	245
Age categorical Units: Subjects			
Adults (18-64 years)	83	82	165
Adults (65-84 years)	40	40	80
Age continuous Units: years			
arithmetic mean	58.6	57.9	
standard deviation	± 11.4	± 12.3	-
Gender categorical Units: Subjects			
Female	40	44	84
Male	83	78	161
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	8	7	15
Not Hispanic or Latino	110	108	218
Unknown or Not Reported	5	7	12
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	0	3	3
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	2	4
White	119	117	236
More than one race	0	0	0
Unknown or Not Reported	1	0	1
Region of Enrollment Units: Subjects			
Greece	10	11	21
Canada	0	4	4
Sweden	1	1	2
Turkey	24	16	40
Belgium	6	5	11

United States	16	8	24
Czechia	7	9	16
Ukraine	18	26	44
Italy	16	7	23
Germany	2	2	4
Spain	23	33	56

End points

End points reporting groups

Reporting group title	12mg/kg Ramucirumab + 80 mg/m² Paclitaxel

Reporting group description:

12 milligram per kilogram (mg/kg) ramucirumab administered intravenously (IV) on day 1 and day 15 (28 day cycles) in combination with 80 milligram per square meter (mg/m²) paclitaxel administered IV on day 1, day 8 and day 15.

Reporting group title	8 mg/kg Ramucirumab + 80 mg/m² Paclitaxel

Reporting group description:

8 mg/kg ramucirumab administered IV on day 1 and day 15 (28 day cycles) in combination with 80 mg/m² paclitaxel administered IV on day 1, day 8 and day 15.

Subject analysis set title	I4T-MC-JVCZ: 12mg/kg Ramucirumab + 80 mg/m² Paclitaxel
Subject analysis set type	Per protocol

Subject analysis set description:

12mg/kg ramucirumab administered intravenously (IV) on day 1 and day 15 (28 day cycles) in combination with 80 mg/m² paclitaxel administered IV on day 1, day 8 and day 15.

Primary: Progression Free Survival (PFS) in Ramucirumab 12mg/kg arm I4T-MC-JVCZ

End point title	Progression Free Survival (PFS) in Ramucirumab 12mg/kg arm I4T-MC-JVCZ[1]

End point description:

PFS was defined as time from the date of randomization(RD) to date of radiographic documentation of progression(RDP) or the date of death due to any cause, whichever is earlier as defined by RECIST v.1.1. Participants with no tumor progression and no death were censored at date of last adequate radiological assessment (AST) or date of RD(whichever is later). This analysis were comparison of PFS for participants treated with ramucirumab 12 mg/kg plus paclitaxel in Study I4T-MC-JVCZ versus placebo plus paclitaxel in I4T-IE-JVBE (NCT01170663) using meta-analysis. Placebo + 80 mg/m² Paclitaxel in I4T-IE-JVBE Number of participants: 335, Median (95% CI), months: 2.86 (2.79 to 3.02). Hazard Ratio (HR) = 0.617, 2 sided Confidence Interval (0.447 to 0.853). HR was estimated by Unstratified cox proportional hazards model comparing Ramucirumab I4T-MC-JVCZ and I4T-IE-JVBE (NCT01170663).

End point type	Primary

End point timeframe:

Randomization to Objective Progressive Disease or Death (Up To 21 Months)
Analysis Population Description (APD). All randomized participants in arm 12mg/kg Ramucirumab + 80 mg/m² Paclitaxel. Censored: Ramucirumab 12 mg/kg + 80 mg/m² Paclitaxel= 25.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis are reported in the outcome measure description. This was a meta-analysis of two studies JVCZ and JVBE. There is no JVBE arm in the participant flow hence comparison data cannot be reported in the statistical analysis section.

End point values	I4T-MC-JVCZ: 12mg/kg Ramucirumab + 80 mg/m² Paclitaxel			
Subject group type	Subject analysis set			
Number of subjects analysed	123			
Units: months				
median (confidence interval 95%)	5.42 (4.40 to 6.01)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) Ramucirumab 12mg/kg Arm and 8mg/kg Arm in I4T-MC-JVCZ

End point title	Progression Free Survival (PFS) Ramucirumab 12mg/kg Arm and 8mg/kg Arm in I4T-MC-JVCZ

End point description:

PFS was defined as time from the date of randomization(RD) to date of radiographic documentation of progression(RDP) or the date of death due to any cause, whichever is earlier as defined by RECIST v.1.1. Participants with no tumor progression and no death were censored at date of last adequate radiological assessment(AST) or date of RD(whichever is later).PD is at least a 20% increase in sum of diameters of target lesions,taking as reference the smallest sum on study.In addition to the relative increase of 20%,the sum must also demonstrate an absolute increase of at least 5 mm.The appearance of 1 or more new lesions is also considered progression.Non-Target PD is unequivocal progression of existing nontarget lesions.A participant with incomplete baseline disease had PFS time censored at the enrollment date.A participant not known to have died or have RDP as of the data inclusion cutoff date for the analysis had PFS time censored at date of the last complete RDP-free disease AST.

End point type	Secondary

End point timeframe:

Randomization to Objective Progressive Disease or Death (Up To 21 Months)

APD: All randomized participants. Censored: Ramucirumab 12 mg/kg + Paclitaxel 80 mg/m2= 25 and 8 mg/kg Ramucirumab + 80 mg/m² Paclitaxel =23.

End point values	12mg/kg Ramucirumab + 80 mg/m² Paclitaxel	8 mg/kg Ramucirumab + 80 mg/m² Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	123	122		
Units: months				
median (confidence interval 95%)	5.42 (4.40 to 6.01)	5.16 (3.81 to 5.65)		

Statistical analyses

Statistical analysis title	Progression Free Survival (PFS) Ramucirumab 12mg/
Comparison groups	12mg/kg Ramucirumab + 80 mg/m² Paclitaxel v 8 mg/kg Ramucirumab + 80 mg/m² Paclitaxel

Number of subjects included in analysis	245
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.963
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.727
upper limit	1.274

Secondary: Pharmacokinetics (PK): Minimum Concentration (Cmin) of Ramucirumab in Combination with Paclitaxel

End point title	Pharmacokinetics (PK): Minimum Concentration (Cmin) of Ramucirumab in Combination with Paclitaxel

End point description:

Pharmacokinetics (PK): Minimum Concentration (Cmin) of Ramucirumab in Combination with Paclitaxel.

Analysis Population Description: All randomized participants who received at least one dose of study drug and had evaluable PK data.

End point type	Secondary

End point timeframe:

Cycle(C) 1 Day(D) 1: Prior to Infusion(PTI),1 to 1.5 hours(hrs) after end of Infusion(EOI); C1 D15: 3 days PTI; C2 D1: 3 days PTI; C2 D15: 3 days PTI,1 to 1.5 hrs after EOI; C3 D1 and 15: 3 days PTI; C4 D1: 3 days PTI and 1 to 1.5 hrs after EOI

End point values	12mg/kg Ramucirumab + 80 mg/m² Paclitaxel	8 mg/kg Ramucirumab + 80 mg/m² Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	95		
Units: Microgram per milliliter (µg/mL)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 15 (Week 2)	39.2 (± 43)	21.4 (± 58)		
Cycle 2 Day 1 (Week 4)	63.6 (± 40)	37.1 (± 50)		
Cycle 2 Day 15 (Week 6)	76.7 (± 42)	43.5 (± 53)		
Cycle 3 Day 1(Week 8)	91.2 (± 40)	51.5 (± 55)		
Cycle 3 Day 15 (Week 10)	99.0 (± 44)	52.9 (± 56)		
Cycle 4 Day 1 (Week 12)	101 (± 55)	56.1 (± 56)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieve Best Overall Tumor Response of

Complete Response (CR) or Partial Response (PR) (Objective Response Rates [ORR])

End point title	Percentage of Participants Who Achieve Best Overall Tumor Response of Complete Response (CR) or Partial Response (PR) (Objective Response Rates [ORR])

End point description:

ORR was defined as the percentage of participants who achieved a PR or CR per RECIST v.1.1.CR is the disappearance of all target lesions.Any pathological lymph nodes(whether target or non-target)must have reduction in short axis to<10mm.Tumor marker results must have normalized.PR is at least a 30% decrease in the sum of diameter of target lesions,taking as reference the baseline sum diameters.ORR is calculated as a total number of participants with CR or PR divided by the total number of participants treated multiplied by 100.

Analysis Population Description: All randomized participants.

End point type	Secondary

End point timeframe:

Baseline to Objective Progressive Disease (Up To 21 Months)

End point values	12mg/kg Ramucirumab + 80 mg/m² Paclitaxel	8 mg/kg Ramucirumab + 80 mg/m² Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	123	122		
Units: percentage of participants				
number (not applicable)	27.6	25.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Exhibit Stable Disease (SD) or Confirmed Response (CR) or Partial Response (PR) [Disease Control Rate (DCR)]

End point title	Percentage of Participants who Exhibit Stable Disease (SD) or Confirmed Response (CR) or Partial Response (PR) [Disease Control Rate (DCR)]

End point description:

DCR is defined as the percentage of participants who achieved CR, PR, or SD per RECIST v.1.1. CR is the disappearance of all target lesions. Any pathological lymph nodes (target or non-target) must have reduction in short axis to <10 mm.Tumor marker results must have normalized. PR is at least a 30% decrease in the sum of diameter of target lesions, taking as reference the baseline sum diameters. SD is defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum diameters while on study. PD is at least a 20% increase in the sum of the diameters of target lesions, taking as reference the smallest sum on study. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm.The appearance of 1 or more new lesions is also considered progression. Non-Target PD is unequivocal progression of existing nontarget lesions. DCR=CR+PR+SD/total number of participants*100.

End point type	Secondary

End point timeframe:

Baseline to Objective Progressive Disease (Up To 21 Months)

Analysis Population Description: All randomized participants.

End point values	12mg/kg Ramucirumab + 80 mg/m² Paclitaxel	8 mg/kg Ramucirumab + 80 mg/m² Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	123	122		
Units: percentage of participants				
number (not applicable)	78.9	75.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Anti-Ramucirumab Antibodies

End point title	Number of Participants with Anti-Ramucirumab Antibodies

End point description:

Participants who had anti-ramucirumab antibodies at postbaseline.

Analysis Population Description: All randomized participants who received at least one dose of study drug and were evaluable for ramucirumab anti-drug antibody.

End point type	Secondary

End point timeframe:

Cycle 1 Predose through Follow-up (Up To 24 Months)

End point values	12mg/kg Ramucirumab + 80 mg/m² Paclitaxel	8 mg/kg Ramucirumab + 80 mg/m² Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	89		
Units: participants	2	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up T0 40 Months

Adverse event reporting additional description:

All randomized participants who received at least one dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	12mg/kg Ramucirumab + 80 mg/m² Paclitaxel

Reporting group description:

12mg/kg ramucirumab administered intravenously (IV) on day 1 and day 15 (28 day cycles) in combination with 80 mg/m² paclitaxel administered IV on day 1, day 8 and day 15.

Reporting group title	8 mg/kg Ramucirumab + 80 mg/m² Paclitaxel

Reporting group description:

8 mg/kg ramucirumab administered IV on day 1 and day 15 (28 day cycles) in combination with 80 mg/m² paclitaxel administered IV on day 1, day 8 and day 15.

Serious adverse events	12mg/kg Ramucirumab + 80 mg/m² Paclitaxel	8 mg/kg Ramucirumab + 80 mg/m² Paclitaxel	
Total subjects affected by serious adverse events			
subjects affected / exposed	47 / 123 (38.21%)	32 / 120 (26.67%)	
number of deaths (all causes)	10	8	
number of deaths resulting from adverse events	5	4	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
lymphangiosis carcinomatosa			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
tumour haemorrhage			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
tumour perforation			
alternative dictionary used:			

MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Vascular disorders			
hypotension			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
shock haemorrhagic			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	2 / 123 (1.63%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
death			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
fatigue			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
general physical health deterioration			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	2 / 123 (1.63%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	2 / 2	0 / 0	
localised oedema			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
malaise			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
oedema			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
organ failure			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
pyrexia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
oedema genital			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
aspiration			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
dyspnoea			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hiccups			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypoxia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
pneumothorax			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pulmonary embolism			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pulmonary hypertension			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
respiratory distress			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Investigations			
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
blood bilirubin increased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	2 / 123 (1.63%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
neutrophil count decreased			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	6 / 123 (4.88%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	6 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
femoral neck fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
infusion related reaction			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
tibia fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
cardiac failure			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
cardiopulmonary failure			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
cardiovascular insufficiency			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
syncope			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	3 / 123 (2.44%)	3 / 120 (2.50%)	
occurrences causally related to treatment / all	2 / 3	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
bone marrow failure			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
febrile neutropenia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	4 / 123 (3.25%)	3 / 120 (2.50%)	
occurrences causally related to treatment / all	4 / 4	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
leukocytosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
neutropenia			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	4 / 123 (3.25%)	2 / 120 (1.67%)	
occurrences causally related to treatment / all	2 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
ascites			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
diarrhoea			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
dysphagia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastric haemorrhage			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	3 / 123 (2.44%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	5 / 6	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastric perforation			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastric stenosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	2 / 123 (1.63%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
haematemesis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ileus			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	2 / 120 (1.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
large intestinal haemorrhage			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
nausea			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

oesophageal fistula			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
oesophageal haemorrhage			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
oesophageal obstruction			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
oesophageal perforation			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumoperitoneum			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
small intestinal obstruction			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
tongue oedema			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
upper gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
vomiting			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	3 / 123 (2.44%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	2 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
cholangitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cholecystitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cholecystitis acute			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
cholelithiasis			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
gallbladder rupture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hepatitis toxic			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
jaundice			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	2 / 123 (1.63%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
proteinuria			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
renal failure			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
bacteraemia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
bronchitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
clostridium difficile colitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
device related infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
enteritis infectious			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
escherichia infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	2 / 123 (1.63%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
lung infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
peritonitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia necrotising			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

respiratory tract infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
sepsis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
septic shock			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metabolism and nutrition disorders			
cachexia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
decreased appetite			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
dehydration			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 123 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hyperkalaemia			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypokalaemia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hyponatraemia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
malnutrition			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 123 (0.81%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	12mg/kg Ramucirumab + 80 mg/m² Paclitaxel	8 mg/kg Ramucirumab + 80 mg/m² Paclitaxel	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	117 / 123 (95.12%)	115 / 120 (95.83%)	
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	14 / 123 (11.38%)	7 / 120 (5.83%)	
occurrences (all)	27	8	
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	20 / 123 (16.26%)	8 / 120 (6.67%)	
occurrences (all)	43	15	

blood alkaline phosphatase increased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	9 / 123 (7.32%)	10 / 120 (8.33%)	
occurrences (all)	25	14	
blood bilirubin increased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	8 / 123 (6.50%)	2 / 120 (1.67%)	
occurrences (all)	12	3	
neutrophil count decreased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	30 / 123 (24.39%)	24 / 120 (20.00%)	
occurrences (all)	91	60	
platelet count decreased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	9 / 123 (7.32%)	7 / 120 (5.83%)	
occurrences (all)	15	13	
weight decreased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	14 / 123 (11.38%)	13 / 120 (10.83%)	
occurrences (all)	16	17	
white blood cell count decreased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	13 / 123 (10.57%)	14 / 120 (11.67%)	
occurrences (all)	33	35	
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	24 / 123 (19.51%)	21 / 120 (17.50%)	
occurrences (all)	44	46	
Nervous system disorders			
dysgeusia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	5 / 123 (4.07%)	9 / 120 (7.50%)	
occurrences (all)	5	13	
headache			

alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	10 / 123 (8.13%)	9 / 120 (7.50%)	
occurrences (all)	12	12	
neuropathy peripheral			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	15 / 123 (12.20%)	15 / 120 (12.50%)	
occurrences (all)	38	22	
paraesthesia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	13 / 123 (10.57%)	13 / 120 (10.83%)	
occurrences (all)	30	29	
peripheral sensory neuropathy			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	8 / 123 (6.50%)	20 / 120 (16.67%)	
occurrences (all)	15	46	
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	34 / 123 (27.64%)	39 / 120 (32.50%)	
occurrences (all)	72	77	
leukopenia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	9 / 123 (7.32%)	9 / 120 (7.50%)	
occurrences (all)	44	18	
neutropenia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	22 / 123 (17.89%)	24 / 120 (20.00%)	
occurrences (all)	78	62	
thrombocytopenia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	7 / 123 (5.69%)	4 / 120 (3.33%)	
occurrences (all)	10	5	
General disorders and administration site conditions			

asthenia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	15 / 123 (12.20%)	19 / 120 (15.83%)	
occurrences (all)	35	49	
fatigue			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	43 / 123 (34.96%)	46 / 120 (38.33%)	
occurrences (all)	85	82	
oedema peripheral			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	10 / 123 (8.13%)	16 / 120 (13.33%)	
occurrences (all)	11	22	
pyrexia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	9 / 123 (7.32%)	8 / 120 (6.67%)	
occurrences (all)	10	8	
Gastrointestinal disorders			
abdominal distension			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	7 / 123 (5.69%)	6 / 120 (5.00%)	
occurrences (all)	9	8	
abdominal pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	20 / 123 (16.26%)	19 / 120 (15.83%)	
occurrences (all)	31	22	
abdominal pain upper			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	8 / 123 (6.50%)	12 / 120 (10.00%)	
occurrences (all)	13	16	
ascites			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	9 / 123 (7.32%)	5 / 120 (4.17%)	
occurrences (all)	11	8	
constipation			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	23 / 123 (18.70%)	21 / 120 (17.50%)	
occurrences (all)	33	27	
diarrhoea			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	31 / 123 (25.20%)	35 / 120 (29.17%)	
occurrences (all)	78	65	
dysphagia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	11 / 123 (8.94%)	4 / 120 (3.33%)	
occurrences (all)	12	4	
nausea			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	27 / 123 (21.95%)	38 / 120 (31.67%)	
occurrences (all)	52	95	
stomatitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	15 / 123 (12.20%)	18 / 120 (15.00%)	
occurrences (all)	19	41	
vomiting			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	29 / 123 (23.58%)	27 / 120 (22.50%)	
occurrences (all)	51	44	
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	14 / 123 (11.38%)	8 / 120 (6.67%)	
occurrences (all)	17	11	
dysphonia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	11 / 123 (8.94%)	6 / 120 (5.00%)	
occurrences (all)	15	7	
dyspnoea			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	4 / 123 (3.25%)	12 / 120 (10.00%)	
occurrences (all)	5	13	
epistaxis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	26 / 123 (21.14%)	28 / 120 (23.33%)	
occurrences (all)	43	36	
Skin and subcutaneous tissue disorders			
alopecia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	19 / 123 (15.45%)	24 / 120 (20.00%)	
occurrences (all)	19	28	
Renal and urinary disorders			
proteinuria			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	9 / 123 (7.32%)	8 / 120 (6.67%)	
occurrences (all)	19	11	
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	8 / 123 (6.50%)	5 / 120 (4.17%)	
occurrences (all)	13	5	
back pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	10 / 123 (8.13%)	9 / 120 (7.50%)	
occurrences (all)	13	14	
myalgia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	11 / 123 (8.94%)	9 / 120 (7.50%)	
occurrences (all)	18	16	
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	25 / 123 (20.33%)	32 / 120 (26.67%)	
occurrences (all)	41	58	
hyperglycaemia			

alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	8 / 123 (6.50%)	11 / 120 (9.17%)	
occurrences (all)	18	20	
hypoalbuminaemia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	10 / 123 (8.13%)	14 / 120 (11.67%)	
occurrences (all)	13	34	
hyponatraemia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	7 / 123 (5.69%)	7 / 120 (5.83%)	
occurrences (all)	13	8	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported