Clinical trial results:
Phase 3 Study of Pemetrexed, Cisplatin, and Radiotherapy Followed by Consolidation Pemetrexed versus Etoposide, Cisplatin, and Radiotherapy Followed by Consolidation Cytotoxic Chemotherapy of Choice in Patients with Unresectable, Locally Advanced, Stage III Non-Small Cell Lung Cancer Other than Predominantly Squamous Cell Histology

Summary

EudraCT number	2008-001170-32
Trial protocol	PT HU ES NL BE FR DE GB IE
Global end of trial date	06 November 2014

Results information

Result version number	v1 (current)
This version publication date	08 June 2016
First version publication date	08 June 2016

Trial information

Trial identification

Sponsor protocol code	H3E-MC-JMIG

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00686959
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Alias : H3E-MC-JMIG, Trial ID: 11514

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, 1 877-CTLilly,
Scientific contact	Available Mon - Fri 9 AM - 5 PM EST , Eli Lilly and Company, 1 877-285-4559,

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	06 November 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 November 2014
Global end of trial reached?	Yes
Global end of trial date	06 November 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To compare the overall survival of patients with locally advanced, Stage III NSCLC of predominantly nonsquamous histology (hereafter simply referred to as nonsquamous) treated with pemetrexed plus cisplatin and concurrent TRT, followed by consolidation chemotherapy with pemetrexed (Arm A) versus etoposide plus cisplatin and concurrent TRT, followed by consolidation with cytotoxic chemotherapy of choice (Arm B).

Protection of trial subjects:

This study was conducted in accordance with International Code of 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:

Thoracic Radiation Therapy (TRT)
Arm A: Pemetrexed + Cisplatin and TRT: Beginning on Day 1 of chemotherapy, once daily fractions (2 Gray [Gy] per day), 5 days a week for 6 weeks and 3 days to target 66 Gy in 33 fractions.
Arm B: Etoposide + Cisplatin and TRT: Beginning on Day 1 of chemotherapy, once daily fractions (2 Gray [Gy] per day), 5 days a week for 6 weeks and 3 days to target 66 Gy in 33 fractions.

Evidence for comparator: -

Actual start date of recruitment	15 September 2008
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	Netherlands: 46
Country: Number of subjects enrolled	Portugal: 18
Country: Number of subjects enrolled	Spain: 65
Country: Number of subjects enrolled	United Kingdom: 19
Country: Number of subjects enrolled	Belgium: 44
Country: Number of subjects enrolled	France: 22
Country: Number of subjects enrolled	Germany: 37
Country: Number of subjects enrolled	Greece: 16
Country: Number of subjects enrolled	Argentina: 3
Country: Number of subjects enrolled	United States: 134
Country: Number of subjects enrolled	Canada: 26
Country: Number of subjects enrolled	Turkey: 7
Country: Number of subjects enrolled	Ireland: 1
Country: Number of subjects enrolled	China: 61

Country: Number of subjects enrolled	Taiwan: 25
Country: Number of subjects enrolled	Brazil: 16
Country: Number of subjects enrolled	Korea, Republic of: 11
Country: Number of subjects enrolled	Australia: 17
Country: Number of subjects enrolled	Mexico: 2
Country: Number of subjects enrolled	India: 28
Worldwide total number of subjects	598
EEA total number of subjects	268

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)	426
From 65 to 84 years	172
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Overall study with two reporting groups. There were 598 participants randomized (Arm A = 301; Arm B = 297), of those participants who were randomized 555 received at least on dose of study drug (Arm A = 283; Arm B = 272) Study completion includes death due to any cause.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Pemetrexed + Cisplatin and Thoracic Radiation Therapy (TRT)

Arm description:

Participants were treated with pemetrexed plus Cisplatin and concurrent TRT ("Concurrent Phase") for three 21-day cycles, followed by a 3-5 week "Recovery Period," then treated with consolidation chemotherapy with pemetrexed ("Consolidation Phase") for up to four 21-day cycles

Arm type	Experimental
Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	LY231514
Other name	Alimta
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pemetrexed: 500 milligrams per meter squared (mg/m^2), intravenous (IV) on Day 1 of each 21-day cycle for 3 cycles.

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

Dosage and administration details:

Cisplatin: 75 mg/m^2, IV on Day 1 of each 21-day cycle x 3 cycles.

Arm title	Etoposide + Csiplatin and TRT

Arm description:

Participants were treated with Etoposide plus Cisplatin and concurrent TRT ("Concurrent Phase") for two 28-day cycles

Arm type	Experimental
Investigational medicinal product name	Etoposide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Etoposide: 50 mg/m^2, IV on Days 1 to 5 and Days 29 to 33

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

Dosage and administration details:

Cisplatin: 50 mg/m^2, IV on Days1, 8, 29, and 36

Number of subjects in period 1	Pemetrexed + Cisplatin and Thoracic Radiation Therapy (TRT)	Etoposide + Csiplatin and TRT
Started	301	297
Received at Least One Dose of Study Drug	283	272
Entered Consolidation Phase	229	202
Completed	177	180
Not completed	124	117
Participants censored (no death events)	124	117

Baseline characteristics

Reporting groups	
Reporting group title	Pemetrexed + Cisplatin and Thoracic Radiation Therapy (TRT)
Reporting group description:	
Participants were treated with pemetrexed plus Cisplatin and concurrent TRT ("Concurrent Phase") for three 21-day cycles, followed by a 3-5 week "Recovery Period," then treated with consolidation chemotherapy with pemetrexed ("Consolidation Phase") for up to four 21-day cycles	
Reporting group title	Etoposide + Csiplatin and TRT
Reporting group description:	
Participants were treated with Etoposide plus Cisplatin and concurrent TRT ("Concurrent Phase") for two 28-day cycles	

Reporting group values	Pemetrexed + Cisplatin and Thoracic Radiation Therapy (TRT)	Etoposide + Csiplatin and TRT	Total
Number of subjects	301	297	598
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)	215	211	426
From 65-84 years	86	86	172
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	124	119	243
Male	177	178	355
Race/ Ethnicity Units: Subjects			
African	15	12	27
Caucasian	217	204	421
East Asian	54	68	122
Hispanic	5	4	9
Native American	1	1	2
West Asian	6	6	12
Missing (unknown)	3	2	5
Eastern Cooperative Oncology Group (ECOG) Performance Status			
0=Fully active, able to carry on all pre-disease performance without restriction 1=Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, such as, light housework, office work			
Units: Subjects			
ECOG 0	148	145	293
ECOG 1	152	149	301

Missing	1	3	4
Disease Stage			
Stage means how big the tumor is and how far it has spread. Stages range from 0 (not spread) to IV (spread throughout the body). Stage IIIA - the cancer has spread to nearby tissue or spread to far away lymph nodes; Stage IIIB - cancer spread to opposite side of chest, more than one tumor within same lobe of lung.			
Units: Subjects			
Stage IIIA	140	142	282
Stage IIIB	161	152	313
Missing	0	3	3
Histology Units: Subjects			
Adenocarcinoma	226	226	452
Large Cell Carcinoma	16	21	37
Other	59	48	107
Missing	0	2	2
Smoking Status			
Smoking history: moderate smoker means </= 15 pack year (PY); heavy smoker means > 15PY.			
Units: Subjects			
Never Smoked	50	58	108
Moderate Smoker	42	38	80
Heavy Smoker	190	183	373
Missing	19	18	37
Baseline Positron Emmission Tomography (PET) Scan			
Participant had a baseline PET scan for staging			
Units: Subjects			
Yes	250	241	491
No	51	56	107

End points

End points reporting groups

Reporting group title	Pemetrexed + Cisplatin and Thoracic Radiation Therapy (TRT)
Reporting group description:	
Participants were treated with pemetrexed plus Cisplatin and concurrent TRT ("Concurrent Phase") for three 21-day cycles, followed by a 3-5 week "Recovery Period," then treated with consolidation chemotherapy with pemetrexed ("Consolidation Phase") for up to four 21-day cycles	
Reporting group title	Etoposide + Csiplatin and TRT
Reporting group description:	
Participants were treated with Etoposide plus Cisplatin and concurrent TRT ("Concurrent Phase") for two 28-day cycles	

Primary: Overall Survival

End point title	Overall Survival
End point description:	
Overall survival (OS) time is from baseline to the date of death from any cause. For participants not known to have died as of the data cut-off date, OS time was censored at the last contact date the participant was known to be alive prior to the data cut-off date. OS was summarized using Kaplan-Meier estimates.	
End point type	Primary
End point timeframe:	
Baseline to Date of Death from Any Cause (Up to 71.4 Months)	

End point values	Pemetrexed + Cisplatin and Thoracic Radiation Therapy (TRT)	Etoposide + Csiplatin and TRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	301	297		
Units: Months				
median (confidence interval 95%)	26.81 (20.4 to 30.92)	24.97 (22.18 to 29.83)		

Statistical analyses

Statistical analysis title	Overall Survival
Statistical analysis description:	
All randomized participants. Arm A had 124 participants censored and Arm B had 117 participants censored.	
Comparison groups	Pemetrexed + Cisplatin and Thoracic Radiation Therapy (TRT) v Etoposide + Csiplatin and TRT

Number of subjects included in analysis	598
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.831
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.2

Secondary: Progression Free Survival

End point title	Progression Free Survival

End point description:

Progression-free survival (PFS) time is from baseline to the first date of documented objective progressive disease (PD) or death from any cause. For participants who were not known to have died or to have had objective PD as of the data inclusion cut-off date for a particular analysis, PFS was censored at the date of the last objective progression-free disease assessments.

End point type	Secondary

End point timeframe:

Baseline to Measured Progressive Disease or Death from Any Cause (Up to 66.6 Months)

End point values	Pemetrexed + Cisplatin and Thoracic Radiation Therapy (TRT)	Etoposide + Csiplatin and TRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	301	297		
Units: Months				
median (confidence interval 95%)	11.37 (10.25 to 13.21)	9.76 (8.38 to 11.73)		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (Complete Response [CR] + Partial Response [PR])

End point title	Objective Response Rate (Complete Response [CR] + Partial Response [PR])

End point description:

Overall response rate (ORR) is the best response of CR or PR as classified by the investigators according to the Response Evaluation Criteria in Solid Tumors (RECIST, v1.1) guidelines. CR is defined as the disappearance of all target and non-target lesions, normalization of tumor marker level of non-target

lesions, and any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 millimeter (mm). PR is an at least 30% decrease in the sum of the diameters of target lesions (taking as reference the baseline sum diameter) without progression of non-target lesions or appearance of new lesions. Overall response rate is calculated as a total number of participants with CR or PR divided by the total number of participants with at least 1 measurable lesion, multiplied by 100.

End point type	Secondary

End point timeframe:

Baseline to Measured Progressive Disease (Up to 7 Months)

End point values	Pemetrexed + Cisplatin and Thoracic Radiation Therapy (TRT)	Etoposide + Csiplatin and TRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	301	297		
Units: Percentage of participants				
number (confidence interval 95%)	35.9 (30.46 to 41.58)	33 (27.67 to 38.66)		

Statistical analyses

No statistical analyses for this end point

Secondary: Survival Rates at 1, 2, and 3 Years

End point title	Survival Rates at 1, 2, and 3 Years

End point description:

The probability that survival time is at least 1, 2, or 3 years was summarized using Kaplan-Meier estimates.

End point type	Secondary

End point timeframe:

Baseline to Date of Death from Any Cause (Up to 71.4 Months)

End point values	Pemetrexed + Cisplatin and Thoracic Radiation Therapy (TRT)	Etoposide + Csiplatin and TRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	301	297		
Units: Probabliity of survival				
number (confidence interval 95%)				
1 year (12months)	0.76 (0.7 to 0.8)	0.77 (0.72 to 0.81)		
2 years (24 months)	0.52 (0.46 to 0.58)	0.52 (0.46 to 0.58)		
3 years (36 months)	0.4 (0.34 to 0.46)	0.37 (0.31 to 0.43)		

Statistical analyses

No statistical analyses for this end point

Secondary: First Site of Disease Failure in Terms of Relapse

End point title	First Site of Disease Failure in Terms of Relapse

End point description:

The percentage of participants with first sites of disease failure in terms of relapse within the radiation treatment field, inside the thorax, (outside of the radiation field), or distant disease are presented. Results were summarized using Kaplan-Meier estimates. Some participants relapsed in more than 1 location/site and appear in more than a single category.

End point type	Secondary

End point timeframe:

Baseline to Relapse (Up to 66.6 Months)

End point values	Pemetrexed + Cisplatin and Thoracic Radiation Therapy (TRT)	Etoposide + Csiplatin and TRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	166[1]	190[2]		
Units: Percentage of participants				
number (confidence interval 95%)				
Relapsed within the radiation treatment field	37.3 (30 to 45.2)	45.8 (38.6 to 53.2)		
Relapsed inside thorax, outside radiation field	20.5 (14.6 to 27.4)	16.3 (11.4 to 22.4)		
Relapsed distant disease	50 (42.2 to 57.8)	45.8 (38.6 to 53.2)		

Notes:

[1] - All randomized participants with objective PD

[2] - All randomized participants with objective PD

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With a Post Baseline Swallowing Diary Score >=4

End point title	Percentage of Participants With a Post Baseline Swallowing Diary Score >=4

End point description:

Participants were provided with a swallowing diary to record issues with swallowing using a 5-point categorical scale: (1) no problems; (2) mild soreness; (3) swallowing solids with some difficulty; (4) inability to swallow solids; and (5) inability to swallow liquids. Participants rated swallowing over the previous 24 hours. The percentage of participants was calculated by dividing the number of with a post

baseline swallowing diary score >=4 by total number of participants analyzed, multiplied by 100.

End point type	Secondary

End point timeframe:

Baseline through 30 Days Post Study

End point values	Pemetrexed + Cisplatin and Thoracic Radiation Therapy (TRT)	Etoposide + Csiplatin and TRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	284[3]	269[4]		
Units: Percentage of participants				
number (confidence interval 95%)	33.8 (26.7 to 37.5)	29 (21.3 to 31.7)		

Notes:

[3] - All randomized participants with at least one post baseline swallowing diary score

[4] - All randomized participants with at least one post baseline swallowing diary score

Statistical analyses

No statistical analyses for this end point

Secondary: Adverse Events: The Number of Deaths Per Treatment Group

End point title	Adverse Events: The Number of Deaths Per Treatment Group

End point description:

The number of deaths that occurred while on study drug, the number of deaths due to adverse events (AEs) while on study drug, and the number of deaths due to the study disease (that is, disease progression) while on study drug are presented. In addition, the number of deaths within 30 days of treatment discontinuation, the number of deaths due to AEs within 30 days of treatment discontinuation, and the number of deaths due to study disease within 30 days of treatment discontinuation are presented. For both the deaths due to AEs that occurred on study and for deaths due to AEs that occurred within 30 days of treatment discontinuation, the causality (events assess as possibly related [poss related] to study drug per investigator judgement) is also presented. A summary of serious and other non-serious adverse events regardless of causality is located in the Reported Adverse Events module.

End point type	Secondary

End point timeframe:

Baseline through 30 Days Post Study

End point values	Pemetrexed + Cisplatin and Thoracic Radiation Therapy (TRT)	Etoposide + Csiplatin and TRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	283[5]	272[6]		
Units: Participants				
number (not applicable)				
On study drug (total)	12	6		
On study drug: Due to AE	10	4		

On study drug: Due to AE possibly related	5	3		
On study drug: Due to study disease	2	0		
Within 30 Days of Discontinuation (disc) (total)	10	6		
Within 30 Days of Disc: Due to AE	5	4		
Within 30 Days of Disc: Due to AE poss related	2	0		
Within 30 Days of Disc: Due to study disease	5	2		

Notes:

[5] - All randomized participants who received at least one dose of study drug.

[6] - All randomized participants who received at least one dose of study drug.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Entire Study	
Adverse event reporting additional description:	
H3E-MC-JMIG	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	Pemetrexed + Cisplatin
Reporting group description: -	
Reporting group title	Etoposide + Cisplatin
Reporting group description: -	

Serious adverse events	Pemetrexed + Cisplatin	Etoposide + Cisplatin	
Total subjects affected by serious adverse events			
subjects affected / exposed	134 / 283 (47.35%)	145 / 272 (53.31%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
lung infiltration malignant			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
malignant melanoma in situ			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
metastases to central nervous system			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	3 / 283 (1.06%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 17	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
paraneoplastic syndrome			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
thyroid cancer			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
tumour haemorrhage			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
tumour pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
deep vein thrombosis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	2 / 272 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
embolism arterial			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypotension			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypovolaemic shock			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
jugular vein thrombosis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
orthostatic hypotension			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
peripheral ischaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
phlebitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

superior vena cava syndrome			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	2 / 272 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
thrombophlebitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
thrombosis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
vena cava thrombosis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 283 (0.71%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
chest pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 283 (1.06%)	5 / 272 (1.84%)	
occurrences causally related to treatment / all	0 / 5	3 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
death			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	2 / 283 (0.71%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
fatigue			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 283 (1.06%)	4 / 272 (1.47%)	
occurrences causally related to treatment / all	2 / 4	3 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
malaise			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 283 (0.71%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
mucosal inflammation			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	1 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
multi-organ failure			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
non-cardiac chest pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

pyrexia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	11 / 283 (3.89%)	4 / 272 (1.47%)	
occurrences causally related to treatment / all	2 / 14	2 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
drug hypersensitivity			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 283 (0.71%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
acute respiratory distress syndrome			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
acute respiratory failure			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 1	
aspiration			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
atelectasis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
bronchial secretion retention			

alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
bronchopleural fistula			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
chronic obstructive pulmonary disease			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cough			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
dyspnoea			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 283 (1.06%)	3 / 272 (1.10%)	
occurrences causally related to treatment / all	0 / 4	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
haemoptysis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	2 / 272 (0.74%)	
occurrences causally related to treatment / all	1 / 2	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypoxia			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pleural effusion			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 283 (1.06%)	2 / 272 (0.74%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia aspiration			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	6 / 283 (2.12%)	3 / 272 (1.10%)	
occurrences causally related to treatment / all	4 / 19	0 / 19	
deaths causally related to treatment / all	2 / 2	0 / 0	
pneumothorax			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 283 (1.06%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pulmonary embolism			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 283 (1.06%)	10 / 272 (3.68%)	
occurrences causally related to treatment / all	0 / 10	2 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
pulmonary haemorrhage			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	

respiratory failure			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 283 (1.06%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	2 / 4	1 / 1	
deaths causally related to treatment / all	2 / 3	1 / 1	
Psychiatric disorders			
confusional state			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 283 (0.71%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
delirium			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
depression			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hallucination			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
blood creatinine increased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 283 (0.71%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	2 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
haemoglobin decreased			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
neutrophil count decreased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	2 / 272 (0.74%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
platelet count decreased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	3 / 272 (1.10%)	
occurrences causally related to treatment / all	0 / 0	3 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
weight decreased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	4 / 283 (1.41%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	2 / 13	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
white blood cell count decreased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	2 / 272 (0.74%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
fall			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
fracture			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hip fracture			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
lumbar vertebral fracture			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
radiation fibrosis - lung			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
radiation oesophagitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	7 / 283 (2.47%)	13 / 272 (4.78%)	
occurrences causally related to treatment / all	6 / 18	8 / 20	
deaths causally related to treatment / all	0 / 0	0 / 0	
radiation pneumonitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	7 / 283 (2.47%)	5 / 272 (1.84%)	
occurrences causally related to treatment / all	3 / 19	1 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
radiation skin injury			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 3	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	

stoma site pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
tracheal haemorrhage			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
aplasia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
tracheo-oesophageal fistula			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
atrial fibrillation			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	4 / 283 (1.41%)	3 / 272 (1.10%)	
occurrences causally related to treatment / all	3 / 11	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
cardiac arrest			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	2 / 272 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
cardiac failure			

alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
cardio-respiratory arrest			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
coronary artery disease			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
endocarditis noninfective			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
myocardial infarction			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 283 (0.71%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	1 / 3	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
pericardial effusion			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pericarditis			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	2 / 283 (0.71%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	1 / 2	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
supraventricular tachycardia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
cerebral infarction			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 11	
deaths causally related to treatment / all	0 / 1	0 / 0	
cerebrovascular accident			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
convulsion			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
dizziness			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 283 (0.71%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
epilepsy			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
intracranial pressure increased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
loss of consciousness			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
migraine			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
paraplegia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
peripheral sensory neuropathy			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
spinal cord compression			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

syncope			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
transient ischaemic attack			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	2 / 272 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 283 (1.06%)	5 / 272 (1.84%)	
occurrences causally related to treatment / all	4 / 6	3 / 22	
deaths causally related to treatment / all	0 / 0	0 / 0	
febrile neutropenia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	12 / 283 (4.24%)	24 / 272 (8.82%)	
occurrences causally related to treatment / all	13 / 14	23 / 25	
deaths causally related to treatment / all	0 / 0	1 / 1	
leukopenia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	4 / 283 (1.41%)	6 / 272 (2.21%)	
occurrences causally related to treatment / all	4 / 6	9 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
lymphopenia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	1 / 1	1 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
neutropenia			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	8 / 283 (2.83%)	13 / 272 (4.78%)	
occurrences causally related to treatment / all	8 / 21	15 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
pancytopenia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	2 / 272 (0.74%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
thrombocytopenia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	5 / 272 (1.84%)	
occurrences causally related to treatment / all	1 / 4	5 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
tinnitus			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
abdominal pain upper			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 1	1 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
anal fistula			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
aorto-oesophageal fistula			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
constipation			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 283 (0.71%)	2 / 272 (0.74%)	
occurrences causally related to treatment / all	1 / 3	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
diarrhoea			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	6 / 283 (2.12%)	5 / 272 (1.84%)	
occurrences causally related to treatment / all	4 / 15	4 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
dyspepsia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
dysphagia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	4 / 283 (1.41%)	5 / 272 (1.84%)	
occurrences causally related to treatment / all	1 / 8	4 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
enteritis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
eructation			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

gastric perforation			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
gastritis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastrointestinal angiodysplasia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastrointestinal ulcer			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 7	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
haematemesis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
ileus			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
intra-abdominal haemorrhage			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
large intestine perforation alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
lower gastrointestinal haemorrhage alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (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 17.1			
subjects affected / exposed	8 / 283 (2.83%)	7 / 272 (2.57%)	
occurrences causally related to treatment / all	8 / 27	6 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
odynophagia alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
oesophageal pain alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
oesophageal perforation alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

oesophagitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	26 / 283 (9.19%)	29 / 272 (10.66%)	
occurrences causally related to treatment / all	21 / 63	19 / 89	
deaths causally related to treatment / all	0 / 0	0 / 0	
oesophagitis ulcerative			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pancreatitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
small intestinal obstruction			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	2 / 272 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
vomiting			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	14 / 283 (4.95%)	8 / 272 (2.94%)	
occurrences causally related to treatment / all	13 / 23	6 / 9	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatobiliary disorders			
cholecystitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
renal failure			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	2 / 283 (0.71%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	2 / 7	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
renal failure acute			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 283 (0.71%)	3 / 272 (1.10%)	
occurrences causally related to treatment / all	2 / 3	3 / 3	
deaths causally related to treatment / all	0 / 0	1 / 1	
renal impairment			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
inappropriate antidiuretic hormone secretion			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
muscle spasms			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
osteoporosis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
atypical pneumonia			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
bacteraemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
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 17.1			
subjects affected / exposed	2 / 283 (0.71%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
bronchopneumonia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	2 / 272 (0.74%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
device related infection			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 283 (0.71%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
diverticulitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastroenteritis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	2 / 272 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

infectious colitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
influenza			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
laryngitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
lobar pneumonia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	1 / 7	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
lower respiratory tract infection			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	3 / 272 (1.10%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
neutropenic infection			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
neutropenic sepsis			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
oral candidiasis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 283 (0.71%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	2 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumocystis jirovecii pneumonia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
pneumonia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	18 / 283 (6.36%)	18 / 272 (6.62%)	
occurrences causally related to treatment / all	10 / 30	6 / 32	
deaths causally related to treatment / all	1 / 2	2 / 4	
pneumonia bacterial			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia haemophilus			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia necrotising			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

pseudomembranous colitis alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pseudomonas infection alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pulmonary tuberculosis alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
respiratory tract infection alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	4 / 283 (1.41%)	2 / 272 (0.74%)	
occurrences causally related to treatment / all	2 / 6	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
sepsis alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	4 / 272 (1.47%)	
occurrences causally related to treatment / all	0 / 2	4 / 5	
deaths causally related to treatment / all	0 / 1	2 / 2	
septic shock alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
upper respiratory tract infection alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	1 / 283 (0.35%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
urinary tract infection			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 283 (0.71%)	2 / 272 (0.74%)	
occurrences causally related to treatment / all	0 / 3	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
varicella			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	0 / 272 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 283 (1.06%)	3 / 272 (1.10%)	
occurrences causally related to treatment / all	5 / 8	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
dehydration			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	7 / 283 (2.47%)	6 / 272 (2.21%)	
occurrences causally related to treatment / all	7 / 15	2 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
hyperglycaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	3 / 272 (1.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypokalaemia			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	0 / 283 (0.00%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypomagnesaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 283 (0.00%)	2 / 272 (0.74%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
hyponatraemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 283 (0.71%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	2 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypovolaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 283 (0.35%)	1 / 272 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Pemetrexed + Cisplatin	Etoposide + Cisplatin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	279 / 283 (98.59%)	269 / 272 (98.90%)	
Vascular disorders			
hypotension			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 283 (1.06%)	16 / 272 (5.88%)	
occurrences (all)	6	40	
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	64 / 283 (22.61%)	35 / 272 (12.87%)	
occurrences (all)	249	101	
chest pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	40 / 283 (14.13%)	32 / 272 (11.76%)	
occurrences (all)	154	71	
fatigue			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	139 / 283 (49.12%)	131 / 272 (48.16%)	
occurrences (all)	685	472	
mucosal inflammation			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	31 / 283 (10.95%)	23 / 272 (8.46%)	
occurrences (all)	73	64	
oedema peripheral			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	24 / 283 (8.48%)	12 / 272 (4.41%)	
occurrences (all)	61	28	
pyrexia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	56 / 283 (19.79%)	42 / 272 (15.44%)	
occurrences (all)	76	60	
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	105 / 283 (37.10%)	84 / 272 (30.88%)	
occurrences (all)	430	273	
dyspnoea			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	93 / 283 (32.86%)	53 / 272 (19.49%)	
occurrences (all)	308	142	
hiccups			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	31 / 283 (10.95%)	17 / 272 (6.25%)	
occurrences (all)	84	33	
oropharyngeal pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	17 / 283 (6.01%)	24 / 272 (8.82%)	
occurrences (all)	43	41	
pneumonitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	23 / 283 (8.13%)	8 / 272 (2.94%)	
occurrences (all)	59	23	
Psychiatric disorders			
anxiety			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	17 / 283 (6.01%)	12 / 272 (4.41%)	
occurrences (all)	61	35	
insomnia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	52 / 283 (18.37%)	42 / 272 (15.44%)	
occurrences (all)	175	126	
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	21 / 283 (7.42%)	11 / 272 (4.04%)	
occurrences (all)	84	25	
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	20 / 283 (7.07%)	9 / 272 (3.31%)	
occurrences (all)	63	18	
blood creatinine increased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	26 / 283 (9.19%)	16 / 272 (5.88%)	
occurrences (all)	67	32	
haemoglobin decreased			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	48 / 283 (16.96%)	43 / 272 (15.81%)	
occurrences (all)	218	155	
neutrophil count decreased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	32 / 283 (11.31%)	31 / 272 (11.40%)	
occurrences (all)	115	76	
platelet count decreased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	24 / 283 (8.48%)	33 / 272 (12.13%)	
occurrences (all)	74	78	
weight decreased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	69 / 283 (24.38%)	61 / 272 (22.43%)	
occurrences (all)	257	204	
white blood cell count decreased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	47 / 283 (16.61%)	43 / 272 (15.81%)	
occurrences (all)	212	131	
Injury, poisoning and procedural complications			
radiation oesophagitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	16 / 283 (5.65%)	18 / 272 (6.62%)	
occurrences (all)	50	42	
radiation pneumonitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	22 / 283 (7.77%)	16 / 272 (5.88%)	
occurrences (all)	52	29	
radiation skin injury			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	45 / 283 (15.90%)	37 / 272 (13.60%)	
occurrences (all)	159	81	
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	50 / 283 (17.67%)	45 / 272 (16.54%)	
occurrences (all)	152	96	
dysgeusia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	31 / 283 (10.95%)	22 / 272 (8.09%)	
occurrences (all)	122	60	
headache			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	36 / 283 (12.72%)	34 / 272 (12.50%)	
occurrences (all)	92	67	
neuropathy peripheral			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	14 / 283 (4.95%)	25 / 272 (9.19%)	
occurrences (all)	35	64	
peripheral sensory neuropathy			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	23 / 283 (8.13%)	21 / 272 (7.72%)	
occurrences (all)	80	61	
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	88 / 283 (31.10%)	94 / 272 (34.56%)	
occurrences (all)	336	312	
leukopenia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	63 / 283 (22.26%)	71 / 272 (26.10%)	
occurrences (all)	267	237	
lymphopenia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	62 / 283 (21.91%)	47 / 272 (17.28%)	
occurrences (all)	297	170	
neutropenia			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	92 / 283 (32.51%)	123 / 272 (45.22%)	
occurrences (all)	252	359	
thrombocytopenia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	39 / 283 (13.78%)	53 / 272 (19.49%)	
occurrences (all)	116	132	
Ear and labyrinth disorders			
tinnitus			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	15 / 283 (5.30%)	8 / 272 (2.94%)	
occurrences (all)	40	27	
Gastrointestinal disorders			
abdominal pain upper			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	35 / 283 (12.37%)	8 / 272 (2.94%)	
occurrences (all)	94	13	
constipation			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	112 / 283 (39.58%)	129 / 272 (47.43%)	
occurrences (all)	312	284	
diarrhoea			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	55 / 283 (19.43%)	63 / 272 (23.16%)	
occurrences (all)	88	104	
dyspepsia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	43 / 283 (15.19%)	37 / 272 (13.60%)	
occurrences (all)	148	95	
dysphagia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	140 / 283 (49.47%)	110 / 272 (40.44%)	
occurrences (all)	567	317	
nausea			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	175 / 283 (61.84%)	144 / 272 (52.94%)	
occurrences (all)	532	365	
odynophagia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	24 / 283 (8.48%)	23 / 272 (8.46%)	
occurrences (all)	103	56	
oesophagitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	119 / 283 (42.05%)	99 / 272 (36.40%)	
occurrences (all)	470	253	
stomatitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	26 / 283 (9.19%)	12 / 272 (4.41%)	
occurrences (all)	50	23	
vomiting			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	110 / 283 (38.87%)	95 / 272 (34.93%)	
occurrences (all)	244	173	
Skin and subcutaneous tissue disorders			
alopecia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	24 / 283 (8.48%)	103 / 272 (37.87%)	
occurrences (all)	110	389	
dry skin			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	12 / 283 (4.24%)	15 / 272 (5.51%)	
occurrences (all)	52	43	
erythema			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	17 / 283 (6.01%)	13 / 272 (4.78%)	
occurrences (all)	50	29	
pruritus			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	18 / 283 (6.36%)	11 / 272 (4.04%)	
occurrences (all)	55	19	
rash			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	45 / 283 (15.90%)	40 / 272 (14.71%)	
occurrences (all)	110	93	
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	13 / 283 (4.59%)	17 / 272 (6.25%)	
occurrences (all)	33	30	
back pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	26 / 283 (9.19%)	21 / 272 (7.72%)	
occurrences (all)	94	51	
myalgia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	15 / 283 (5.30%)	11 / 272 (4.04%)	
occurrences (all)	41	17	
pain in extremity			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	11 / 283 (3.89%)	14 / 272 (5.15%)	
occurrences (all)	26	30	
Infections and infestations			
pneumonia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	17 / 283 (6.01%)	12 / 272 (4.41%)	
occurrences (all)	36	21	
upper respiratory tract infection			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	15 / 283 (5.30%)	11 / 272 (4.04%)	
occurrences (all)	29	18	
Metabolism and nutrition disorders			

decreased appetite			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	104 / 283 (36.75%)	88 / 272 (32.35%)	
occurrences (all)	366	228	
dehydration			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	19 / 283 (6.71%)	24 / 272 (8.82%)	
occurrences (all)	31	38	
hyperglycaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	16 / 283 (5.65%)	8 / 272 (2.94%)	
occurrences (all)	57	25	
hypokalaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	20 / 283 (7.07%)	32 / 272 (11.76%)	
occurrences (all)	43	49	
hypomagnesaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	22 / 283 (7.77%)	32 / 272 (11.76%)	
occurrences (all)	84	84	
hyponatraemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	19 / 283 (6.71%)	22 / 272 (8.09%)	
occurrences (all)	52	55	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 January 2009	Amendment (a): Change to inclusion/exclusion criteria
22 July 2009	Amendment (b): Change to inclusion/exclusion criteria
30 July 2010	Amendment (c): Change to inclusion/exclusion criteria
03 October 2011	Amendment (e): Scientific values of the study

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
02 September 2012	Enrollment was stopped for futility at a point when 598 (99.7%) participants targeted for accrual had been enrolled. The result of the futility analysis suggested that Arm A would not meet the primary endpoint of improvement in Overall Survival over Arm B. No new safety issues were identified during the study and participants who had been randomized and were on active treatment at the time of enrollment closure were allowed to continue with their assigned study therapy.	-

Notes:

Limitations and caveats

None reported