Clinical trial results:
A phase 2 study of Pemetrexed and Cisplatin plus Cetuximab followed by Pemetrexed and Cetuximab Maintenance Therapy in Patients with Locally Advanced or Metastatic Non-Small Cell Lung Cancer (Stage IIIB or IV) other than Predominantly Squamous Cell Histology

Summary

EudraCT number	2008-004330-24
Trial protocol	DE AT NL ES IT GR
Global end of trial date	19 September 2014

Results information

Result version number	v1 (current)
This version publication date	15 April 2016
First version publication date	15 April 2016

Trial information

Trial identification

Sponsor protocol code	H3E-MC-S104

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00867009
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Alias: H3E-MC-S104, Trial ID: 10726

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, 1 800-CTLilly,
Scientific contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 800-285-4559,
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, 1 800-CTLilly,
Scientific contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 800-285-4559,

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	No

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 September 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 May 2011
Global end of trial reached?	Yes
Global end of trial date	19 September 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study will estimate the response rate in patients with advanced or metastatic non-squamous Non-Small Cell Lung Cancer. Patients who don't progress after 4 to 6 cycles of induction treatment with pemetrexed, cisplatin and cetuximab will receive maintenance treatment with pemetrexed and cetuximab.

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: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Greece: 12
Country: Number of subjects enrolled	Spain: 25
Country: Number of subjects enrolled	Austria: 6
Country: Number of subjects enrolled	Germany: 28
Country: Number of subjects enrolled	Netherlands: 16
Country: Number of subjects enrolled	Italy: 26
Worldwide total number of subjects	113
EEA total number of subjects	113

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	84
From 65 to 84 years	29
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

No text entered

Pre-assignment

Screening details:

No text entered

Period 1

Period 1 title	Induction Period
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Pem/Cis + Cet

Arm description:

Induction Therapy: 500 milligrams per meter squared (mg/m²) pemetrexed (Pem)on Day 1 of every 21-day cycle, 75 mg/m² cisplatin (Cis) on Day 1 of every 21-day cycle and 400 mg/m² cetuximab (Cet) given intravenously (IV) on Day 1 of Cycle 1 and 250 mg/m² once weekly thereafter. Induction period is 4 to 6 cycles.

Maintenance Therapy: 500 mg/m² pemetrexed (Pem) given intravenously (IV) on Day 1 of each 21 day cycle and 250 mg/m² cetuximab (Cet) given weekly until progressive disease (PD) or treatment discontinuation.

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:

Induction therapy: 500 mg/m², intravenous, on Day 1 of each 21-day cycle for 4 to 6 cycles

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

Dosage and administration details:

Induction therapy: 75 mg/m², intravenous, on Day 1 of each 21-day cycle for 4 to 6 cycles

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

Dosage and administration details:

Induction therapy: Loading dose of 400 mg/m², intravenous, on Day 1 of cycle 1, then 250 mg/m², intravenous, weekly for 4 to 6 cycles, 21 day cycles

Number of subjects in period 1	Pem/Cis + Cet
Started	113
Received at least 1 dose of study drug	113
Protocol Qualified (PQ) Population	109
Completed	51
Not completed	62
Consent withdrawn by subject	8
Physician decision	3
Death due to serious adverse event	6
Progressive Disease (PD)	25
Nonserious Adverse Event	5
Death due to Study Disease	4
Serious Adverse Event	10
Protocol deviation	1

Period 2

Period 2 title	Maintenance Period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Pem/Cis + Cet

Arm description:

Induction Therapy: 500 mg/m² pemetrexed (Pem)on Day 1 of every 21-day cycle, 75 mg/m² cisplatin (Cis) on Day 1 of every 21-day cycle and 400 mg/m² cetuximab (Cet) given intravenously (IV) on Day 1 of Cycle 1 and 250 mg/m² once weekly thereafter. Induction period is 4 to 6 cycles.

Maintenance Therapy: 500 mg/m² pemetrexed (Pem) given intravenously (IV) on Day 1 of each 21 day cycle and 250 mg/m² cetuximab (Cet) given weekly until progressive disease (PD) or treatment discontinuation.

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:

Maintenance therapy: 500 mg/m², intravenous, on Day 1 of each 21-day cycle until progressive disease or treatment discontinuation

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

Dosage and administration details:

Maintenance therapy: 250 mg/m², intravenous, weekly until progressive disease or treatment discontinuation

Number of subjects in period 2	Pem/Cis + Cet
Started	51
Completed	47
Not completed	4
On-going in the Study at Data Cut-off	4

Baseline characteristics

Reporting groups	
Reporting group title	Pem/Cis + Cet

Reporting group description:

Induction Therapy: 500 milligrams per meter squared (mg/m²) pemetrexed (Pem)on Day 1 of every 21-day cycle, 75 mg/m² cisplatin (Cis) on Day 1 of every 21-day cycle and 400 mg/m² cetuximab (Cet) given intravenously (IV) on Day 1 of Cycle 1 and 250 mg/m² once weekly thereafter. Induction period is 4 to 6 cycles.

Maintenance Therapy: 500 mg/m² pemetrexed (Pem) given intravenously (IV) on Day 1 of each 21 day cycle and 250 mg/m² cetuximab (Cet) given weekly until progressive disease (PD) or treatment discontinuation.

Reporting group values	Pem/Cis + Cet	Total	
Number of subjects	113	113	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	84	84	
From 65-84 years	29	29	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	59.15		
standard deviation	± 8.83	-	
Gender, Male/Female Units: participants			
Female	41	41	
Male	72	72	
Race/Ethnicity, Customized Units: Subjects			
White	113	113	
Region of Enrollment Units: Subjects			
Greece	12	12	
Spain	25	25	
Austria	6	6	
Germany	28	28	
Netherlands	16	16	
Italy	26	26	
Eastern Co-operative Oncology Group (ECOG) Performance Status			
Classifies patients according to their functional impairment. ECOG Performance Score: 0 - Fully Active; 1 - Ambulatory, Restricted Strenuous Activity; 2 - Ambulatory, No Work Activities; 3 - Partially Confined			

to Bed, Limited Self Care; 4 - Completely Disabled; 5 - Death			
Units: Subjects			
0 - Fully Active	56	56	
1 - Ambulatory, Restricted Strenuous Activity	57	57	
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 IIIB - the cancer has spread to nearby tissue or spread to far away lymph nodes. Stage IV - the cancer has spread to other organs of the body such as the other lung, brain, or liver			
Units: Subjects			
Stage IIIB	9	9	
Stage IV	104	104	
Pathological Diagnosis Units: Subjects			
Adenocarcinoma (Adeno), Breast	1	1	
Carcinoma, Adenosquamous,Lung, Predominantly Adeno	1	1	
Large Cells Lung Carcinoma	5	5	
Malignant Neoplasm, Adeno Lung	88	88	
Non-Small Cell Lung (NSCL) Cancer	9	9	
Poorly Differentiated Non-Small Cell	8	8	
Missing	1	1	

End points

End points reporting groups

Reporting group title	Pem/Cis + Cet

Reporting group description:

Induction Therapy: 500 milligrams per meter squared (mg/m²) pemetrexed (Pem)on Day 1 of every 21-day cycle, 75 mg/m² cisplatin (Cis) on Day 1 of every 21-day cycle and 400 mg/m² cetuximab (Cet) given intravenously (IV) on Day 1 of Cycle 1 and 250 mg/m² once weekly thereafter. Induction period is 4 to 6 cycles.

Maintenance Therapy: 500 mg/m² pemetrexed (Pem) given intravenously (IV) on Day 1 of each 21 day cycle and 250 mg/m² cetuximab (Cet) given weekly until progressive disease (PD) or treatment discontinuation.

Reporting group title	Pem/Cis + Cet

Reporting group description:

Induction Therapy: 500 mg/m² pemetrexed (Pem)on Day 1 of every 21-day cycle, 75 mg/m² cisplatin (Cis) on Day 1 of every 21-day cycle and 400 mg/m² cetuximab (Cet) given intravenously (IV) on Day 1 of Cycle 1 and 250 mg/m² once weekly thereafter. Induction period is 4 to 6 cycles.

Maintenance Therapy: 500 mg/m² pemetrexed (Pem) given intravenously (IV) on Day 1 of each 21 day cycle and 250 mg/m² cetuximab (Cet) given weekly until progressive disease (PD) or treatment discontinuation.

Subject analysis set title	Received at Least One Dose of Study Drug
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants with Stage IIIB/IV non-squamous (NS) non-small cell lung cancer (NSCLC)

Subject analysis set title	Protocol Qualified (PQ) Population
Subject analysis set type	Per protocol

Subject analysis set description:

Stage IIIB/IV NS-NSCLC, no concurrent chemotherapy, measurable disease, ≥1 dose study drug.

Subject analysis set title	Completed Induction Period
Subject analysis set type	Per protocol

Subject analysis set description:

Participants continued on the study in the Maintenance Period.

Primary: Percentage of participants with a tumor response (objective tumor response rate)

End point title	Percentage of participants with a tumor response (objective tumor response rate)[1]

End point description:

Response was assessed using Response Evaluation Criteria In Solid Tumors (RECIST) criteria. Complete Response (CR)=disappearance of all target lesions; Partial Response (PR)=30% decrease in sum of longest diameter of target lesions. Tumor response is presented as a percentage (%) and is the number of participants with a CR plus PR divided by the number of participants in the protocol qualified (PQ) population, then multiplied by 100.

End point type	Primary

End point timeframe:

From start of treatment until documented best response (up to 18.9 months)

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: Descriptive statistics are used to represent the tumor response rate as there are no comparison groups for this single arm study. The Overall Response Rate was 38.5% of the Protocol Qualified (PQ) population with an 80% Confidence Interval (CI).

End point values	Protocol Qualified (PQ) Population			
Subject group type	Subject analysis set			
Number of subjects analysed	109			
Units: Percentage of participants				
number (not applicable)				
Percentage of Participants With a Tumor Response	38.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS)

End point title	Progression-free Survival (PFS)

End point description:

PFS is measured from study entry until disease progression, death or date of last contact. Progressive disease (PD) was determined using Response Evaluation Criteria In Solid Tumors (RECIST) criteria. PD = 20% increase in sum of longest diameter of target lesions or the appearance of 1 or more new lesions and/or unequivocal progression of existing non-target lesions. For participants not known to have died or have had objective PD as of the data cutoff date, PFS was censored at the date of the last objective progression-free disease assessment.

End point type	Secondary

End point timeframe:

From start of treatment until documented disease progression or death from any cause (up to 18.9 months)

End point values	Protocol Qualified (PQ) Population			
Subject group type	Subject analysis set			
Number of subjects analysed	109			
Units: Months				
median (full range (min-max))				
Progression-free Survival (PFS)	5.82 (0.03 to 18.89)			

Statistical analyses

No statistical analyses for this end point

Secondary: The Percentage of Participants Still Living at One Year (One Year Survival Rate)

End point title	The Percentage of Participants Still Living at One Year (One Year Survival Rate)

End point description:

The one year survival rate is presented as percentage (%) of participants still living at one year and is

the number of participants that are still alive at one year divided by the number of participants in the protocol qualified (PQ) population, which is then multiplied by 100.

End point type	Secondary

End point timeframe:

One year

End point values	Protocol Qualified (PQ) Population			
Subject group type	Subject analysis set			
Number of subjects analysed	109			
Units: Percentage of participants				
number (not applicable)				
Percentage of Participants Still Living at 1 Year	45			

Statistical analyses

No statistical analyses for this end point

Secondary: The Percentage of Participants With Complete Response (CR), Partial Response (PR) or Stable Disease (SD) (Disease Control Rate [DCR])

End point title	The Percentage of Participants With Complete Response (CR), Partial Response (PR) or Stable Disease (SD) (Disease Control Rate [DCR])

End point description:

The DCR is presented as percentage (%) and is the number of participants with a best tumor response of CR, PR, or SD divided by the number of participants in the protocol qualified (PQ) population, then multiplied by 100. Best tumor response of CR, PR, or SD was determined from the sequence of tumor response assessments. Tumor response was assessed using RECIST criteria. CR=disappearance of all target lesions; PR=30% decrease in sum of longest diameter of target lesions; SD=small changes that do not meet above criteria.

End point type	Secondary

End point timeframe:

From start of treatment until documented best tumor response (up to 18.9 months)

End point values	Protocol Qualified (PQ) Population			
Subject group type	Subject analysis set			
Number of subjects analysed	109			
Units: Percentage of participants				
number (not applicable)				
Percentage of participants with response	59.6			

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-S104	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	Pemetrexed and Cisplatin plus Cetuximab

Reporting group description: -

Serious adverse events	Pemetrexed and Cisplatin plus Cetuximab		
Total subjects affected by serious adverse events			
subjects affected / exposed	61 / 113 (53.98%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
tumour pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
deep vein thrombosis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
peripheral ischaemia			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	2 / 113 (1.77%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
thrombosis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
venous thrombosis limb				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
chest pain				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
chills				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
death				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
device occlusion				
alternative dictionary used: MedDRA 17.1				

subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
fatigue				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
general physical health deterioration				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	3 / 113 (2.65%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 2			
mucosal inflammation				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
malaise				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
obstruction				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
pain				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

oedema peripheral				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
pyrexia				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
sudden death				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 1			
Immune system disorders				
cytokine release syndrome				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
drug hypersensitivity				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
hypersensitivity				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
uterine haemorrhage				

alternative dictionary used: MedDRA 17.1				
subjects affected / exposed[1]	1 / 41 (2.44%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
dyspnoea				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	3 / 113 (2.65%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
hypoxia				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
pleural effusion				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	3 / 113 (2.65%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
pulmonary embolism				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	6 / 113 (5.31%)			
occurrences causally related to treatment / all	1 / 6			
deaths causally related to treatment / all	0 / 2			
Psychiatric disorders				
confusional state				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
alanine aminotransferase increased				

alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
aspartate aminotransferase increased				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
haemoglobin decreased				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 1			
neutrophil count decreased				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
white blood cell count decreased				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
atrial flutter				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
intracardiac thrombus				
alternative dictionary used: MedDRA 17.1				

subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
myocardial ischaemia				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
tachyarrhythmia				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
cerebral ischaemia				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
convulsion				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
dizziness				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
hemiparesis				
alternative dictionary used: MedDRA 17.1				

subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
leukoencephalopathy			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
nerve compression			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
tremor			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	6 / 113 (5.31%)		
occurrences causally related to treatment / all	6 / 6		
deaths causally related to treatment / all	0 / 0		
febrile neutropenia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
leukopenia			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	3 / 113 (2.65%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 1			
neutropenia				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	6 / 113 (5.31%)			
occurrences causally related to treatment / all	6 / 6			
deaths causally related to treatment / all	0 / 0			
thrombocytopenia				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	5 / 113 (4.42%)			
occurrences causally related to treatment / all	7 / 7			
deaths causally related to treatment / all	0 / 1			
Ear and labyrinth disorders				
vertigo				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
diplopia				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
abdominal pain				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
constipation				
alternative dictionary used: MedDRA 17.1				

subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
diarrhoea				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	3 / 113 (2.65%)			
occurrences causally related to treatment / all	3 / 4			
deaths causally related to treatment / all	0 / 0			
diverticular perforation				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
duodenal ulcer				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
duodenal perforation				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ileus				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
large intestine perforation				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 1			

nausea				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
rectal haemorrhage				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
stomatitis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
vomiting				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	5 / 113 (4.42%)			
occurrences causally related to treatment / all	4 / 5			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
rash				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
stasis dermatitis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
renal failure				
alternative dictionary used: MedDRA 17.1				

subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
bone pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
appendicitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
biliary sepsis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
catheter site infection			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
diverticulitis			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
erysipelas				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
enterococcal sepsis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
gastroenteritis norovirus				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
gangrene				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
herpes zoster				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
infection				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			

peritonitis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
pneumonia				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
sepsis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
decreased appetite				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
hypocalcaemia				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
hypokalaemia				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Pemetrexed and Cisplatin plus Cetuximab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	101 / 113 (89.38%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
basal cell carcinoma			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
uterine leiomyoma			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed[2]	1 / 41 (2.44%)		
occurrences (all)	1		
Vascular disorders			
deep vein thrombosis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
flushing			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
hot flush			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
hypertension			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	5		
hypotension			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	4		
phlebitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
phlebitis superficial			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Surgical and medical procedures			
catheter placement			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
dental implantation			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	15 / 113 (13.27%)		
occurrences (all)	20		
catheter site pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
chills			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
chest pain			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	8 / 113 (7.08%)			
occurrences (all)	8			
extravasation				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
feeling cold				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	2			
fatigue				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	37 / 113 (32.74%)			
occurrences (all)	81			
facial pain				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
generalised oedema				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
hernia				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
influenza like illness				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
localised oedema				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	2			

malaise				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
mucosal dryness				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
mucosal inflammation				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	21 / 113 (18.58%)			
occurrences (all)	30			
oedema peripheral				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	9 / 113 (7.96%)			
occurrences (all)	12			
pain				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	2			
peripheral swelling				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
pyrexia				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	14 / 113 (12.39%)			
occurrences (all)	19			
ulcer				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
Immune system disorders				

contrast media allergy			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
drug hypersensitivity			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
hypersensitivity			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	4		
seasonal allergy			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Reproductive system and breast disorders			
balanoposthitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed[3]	1 / 72 (1.39%)		
occurrences (all)	1		
erectile dysfunction			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed[4]	1 / 72 (1.39%)		
occurrences (all)	1		
menstruation irregular			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed[5]	1 / 41 (2.44%)		
occurrences (all)	1		
uterine haemorrhage			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed[6]	1 / 41 (2.44%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			

cough				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	20 / 113 (17.70%)			
occurrences (all)	24			
dyspnoea				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	18 / 113 (15.93%)			
occurrences (all)	28			
dysphonia				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	6 / 113 (5.31%)			
occurrences (all)	7			
epistaxis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	7 / 113 (6.19%)			
occurrences (all)	7			
dyspnoea exertional				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	2			
haemoptysis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
hiccups				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	4 / 113 (3.54%)			
occurrences (all)	4			
hypoxia				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
laryngospasm				
alternative dictionary used: MedDRA 17.1				

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
oropharyngeal pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
pharyngeal ulceration			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
pleuritic pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
productive cough			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
pulmonary embolism			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
rhinitis allergic			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	3		
sleep apnoea syndrome			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Psychiatric disorders			
anxiety			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
confusional state			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	4		
depression			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	4		
fear			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
insomnia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	5		
sleep disorder			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Investigations			
activated partial thromboplastin time prolonged			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
alanine aminotransferase increased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	6 / 113 (5.31%)		
occurrences (all)	13		
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	4 / 113 (3.54%)			
occurrences (all)	17			
blood calcium				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
blood calcium decreased				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
blood creatinine decreased				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
blood sodium decreased				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
blood potassium decreased				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
blood magnesium decreased				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	4 / 113 (3.54%)			
occurrences (all)	6			
blood creatinine increased				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	5 / 113 (4.42%)			
occurrences (all)	8			
gamma-glutamyltransferase increased				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	6			

glomerular filtration rate decreased				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
haemoglobin decreased				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	11 / 113 (9.73%)			
occurrences (all)	20			
haemoglobin				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
neutrophil count decreased				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	3 / 113 (2.65%)			
occurrences (all)	4			
platelet count decreased				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	6 / 113 (5.31%)			
occurrences (all)	8			
protein c increased				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
weight increased				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	2			
white blood cell count decreased				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	3 / 113 (2.65%)			
occurrences (all)	5			
weight decreased				
alternative dictionary used: MedDRA 17.1				

subjects affected / exposed	11 / 113 (9.73%)		
occurrences (all)	11		
Injury, poisoning and procedural complications			
bone contusion			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
fracture			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
head injury			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
radiation skin injury			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
radius fracture			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
thermal burn			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
upper limb fracture			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
vascular injury			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
wound			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Cardiac disorders			
angina pectoris			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
atrial fibrillation			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
cardiac failure			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
cardiac fibrillation			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
palpitations			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
sinus tachycardia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
tachycardia			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Nervous system disorders			
ageusia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
ataxia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
cerebral ischaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
dizziness			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	15 / 113 (13.27%)		
occurrences (all)	15		
dysgeusia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	8 / 113 (7.08%)		
occurrences (all)	9		
dysarthria			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
headache			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	9 / 113 (7.96%)		
occurrences (all)	15		
hypogeusia			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	2			
neuralgia				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	2			
neuropathy peripheral				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	3 / 113 (2.65%)			
occurrences (all)	3			
paraesthesia				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	3 / 113 (2.65%)			
occurrences (all)	4			
paraparesis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
peripheral sensory neuropathy				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	12 / 113 (10.62%)			
occurrences (all)	14			
peripheral motor neuropathy				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	2			
presyncope				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
somnolence				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			

tremor			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	20 / 113 (17.70%)		
occurrences (all)	38		
febrile neutropenia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
haemoglobinaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
lymphopenia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
leukopenia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	24 / 113 (21.24%)		
occurrences (all)	60		
neutropenia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	25 / 113 (22.12%)		
occurrences (all)	72		
thrombocytopenia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	7 / 113 (6.19%)		
occurrences (all)	9		
Ear and labyrinth disorders			

deafness			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	5		
ear haemorrhage			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
external ear pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
hypoacusis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
tinnitus			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	5		
vertigo			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	3		
Eye disorders			
blepharitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
diplopia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
dry eye			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	5		
eye oedema			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
eyelid disorder			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
lacrimation increased			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	10 / 113 (8.85%)		
occurrences (all)	12		
keratitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
ocular surface disease			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
ocular hyperaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
ulcerative keratitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Gastrointestinal disorders			
abdominal pain upper			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	5 / 113 (4.42%)			
occurrences (all)	8			
abdominal distension				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	2			
abdominal pain				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	7 / 113 (6.19%)			
occurrences (all)	8			
cheilitis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
constipation				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	29 / 113 (25.66%)			
occurrences (all)	33			
diarrhoea				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	24 / 113 (21.24%)			
occurrences (all)	36			
dry mouth				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	5 / 113 (4.42%)			
occurrences (all)	5			
dysphagia				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	8 / 113 (7.08%)			
occurrences (all)	9			
dyspepsia				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	8 / 113 (7.08%)			
occurrences (all)	8			

eructation				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	2			
gastritis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	6 / 113 (5.31%)			
occurrences (all)	9			
glossodynia				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
glossitis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
gastrointestinal ulcer				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
gastrointestinal haemorrhage				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
haemorrhoids				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	2			
nausea				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	51 / 113 (45.13%)			
occurrences (all)	95			
odynophagia				
alternative dictionary used: MedDRA 17.1				

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
oesophagitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	3		
rectal haemorrhage			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
stomatitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	23 / 113 (20.35%)		
occurrences (all)	38		
vomiting			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	34 / 113 (30.09%)		
occurrences (all)	58		
Hepatobiliary disorders			
cholangitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
hepatic pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
hyperbilirubinaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
hypertransaminasaemia			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
acne			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
actinic keratosis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
alopecia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	8 / 113 (7.08%)		
occurrences (all)	10		
dermatitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
dermatitis acneiform			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	7 / 113 (6.19%)		
occurrences (all)	7		
dry skin			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	11 / 113 (9.73%)		
occurrences (all)	12		
erythema			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
exfoliative rash			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	2			
erythema multiforme				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	3 / 113 (2.65%)			
occurrences (all)	4			
hirsutism				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed[7]	1 / 41 (2.44%)			
occurrences (all)	1			
hyperhidrosis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	3			
hypertrichosis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	2			
intertrigo				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
nail disorder				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	6 / 113 (5.31%)			
occurrences (all)	7			
nail toxicity				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
palmar-plantar erythrodysaesthesia syndrome				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	7 / 113 (6.19%)			
occurrences (all)	12			

pain of skin				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
pruritus				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	3 / 113 (2.65%)			
occurrences (all)	3			
rash				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	62 / 113 (54.87%)			
occurrences (all)	88			
rash follicular				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
skin disorder				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
skin fissures				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	2			
skin reaction				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	2			
skin hyperpigmentation				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	3 / 113 (2.65%)			
occurrences (all)	3			
Renal and urinary disorders				

bladder pain				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
bladder spasm				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
haematuria				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
nephropathy toxic				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
pollakiuria				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	2			
renal failure				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	2			
renal colic				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
urinary retention				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
Endocrine disorders				

inappropriate antidiuretic hormone secretion			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	5		
back pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	10 / 113 (8.85%)		
occurrences (all)	19		
bone pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
intervertebral disc space narrowing			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
muscle spasms			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
musculoskeletal pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
myalgia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	7 / 113 (6.19%)		
occurrences (all)	13		
musculoskeletal chest pain			

alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	4 / 113 (3.54%)			
occurrences (all)	4			
neck pain				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	2			
pain in extremity				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	3 / 113 (2.65%)			
occurrences (all)	3			
trismus				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
Infections and infestations				
bronchitis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	2			
cellulitis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
cystitis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	2			
conjunctivitis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	16 / 113 (14.16%)			
occurrences (all)	25			
ear infection				
alternative dictionary used: MedDRA 17.1				

subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
eye infection				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	2			
folliculitis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	5 / 113 (4.42%)			
occurrences (all)	5			
gastroenteritis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
herpes simplex				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	2			
influenza				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
infection				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	2			
laryngitis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
localised infection				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			

nail bed infection				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
nail infection				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	5 / 113 (4.42%)			
occurrences (all)	6			
nasopharyngitis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	4 / 113 (3.54%)			
occurrences (all)	4			
oropharyngeal candidiasis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
oral candidiasis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
oral fungal infection				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
paronychia				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	2			
penile infection				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed[8]	1 / 72 (1.39%)			
occurrences (all)	3			
pharyngitis				
alternative dictionary used: MedDRA 17.1				

subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
pneumonia				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
respiratory tract infection				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	4 / 113 (3.54%)			
occurrences (all)	5			
rhinitis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	3			
sinusitis				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	3			
skin infection				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences (all)	2			
tooth infection				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
upper aerodigestive tract infection				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			
upper respiratory tract infection				
alternative dictionary used: MedDRA 17.1				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences (all)	1			

vaginal infection			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed[9]	2 / 41 (4.88%)		
occurrences (all)	2		
urinary tract infection			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	5		
Metabolism and nutrition disorders			
cachexia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
decreased appetite			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	21 / 113 (18.58%)		
occurrences (all)	34		
dehydration			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
fluid retention			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	8		
hyperglycaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	6		
hyperkalaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
hypernatraemia			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
hypocalcaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	8 / 113 (7.08%)		
occurrences (all)	12		
hypoalbuminaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
hypokalaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	6		
hypomagnesaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	8 / 113 (7.08%)		
occurrences (all)	8		
hyponatraemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	3		

Notes:

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.
[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.
[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None reported

Notes: