Clinical trial results:
A Randomized, Multicenter, Open-Label, Phase 2 Study of Paclitaxel-Carboplatin Chemotherapy Plus Necitumumab (IMC-11F8) Versus Paclitaxel-Carboplatin Chemotherapy Alone in the First-Line Treatment of Patients With Stage IV Squamous Non-Small Cell Lung Cancer (NSCLC)

Summary

EudraCT number	2012-003214-13
Trial protocol	DE
Global end of trial date	14 July 2017

Results information

Result version number	v1 (current)
This version publication date	30 July 2018
First version publication date	30 July 2018

Trial information

Trial identification

Sponsor protocol code	I4X-MC-JFCL

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01769391
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 14790

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center , Indianapolis, 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	14 July 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 July 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study is to evaluate if necitumumab added to standard chemotherapy of paclitaxel and carboplatin is more effective to treat cancer than the standard chemotherapy of paclitaxel and carboplatin alone.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 January 2013
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	Russian Federation: 40
Country: Number of subjects enrolled	United States: 78
Country: Number of subjects enrolled	Poland: 19
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 16
Country: Number of subjects enrolled	Mexico: 6
Country: Number of subjects enrolled	Germany: 8
Worldwide total number of subjects	167
EEA total number of subjects	27

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)	75
From 65 to 84 years	90
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A completer is defined as having a complete radiographic assessment at baseline and at least one complete post-baseline radiographic assessment of CR, PR , SD or PD.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Necitumumab +Paclitaxel+Carboplatin

Arm description:

Necitumumab 800 milligram (mg) administered intravenously (IV) on Days 1 and 8 of every 3 week cycle.
Paclitaxel 200 mg per square meter (mg/m²) administered IV on Day 1 of every 3 week cycle.
Carboplatin AUC6 administered IV on Day 1 of every 3 week cycle.

Arm type	Experimental
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel 200 milligram per square meter (mg/m²) administered IV on Day 1 of every 3 week cycle.

Investigational medicinal product name	Necitumumab
Investigational medicinal product code	
Other name	LY3012211, IMC-11F8
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Necitumumab 800 milligram (mg) administered intravenously (IV) on Days 1 and 8 of every 3 week cycle.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin Area Under the Curve (AUC)6 milligrams times minute per milliliter (mg•min/mL) administered IV on Day 1 of every 3 week cycle.

Arm title	Paclitaxel + Carboplatin

Arm description:

Paclitaxel 200 mg/m² administered IV on Day 1 of every 3 week cycle.
Carboplatin AUC6 administered IV on Day 1 of every 3 week cycle.
The combination of paclitaxel-carboplatin may continue for a maximum of 6 cycles.

Arm type	Active comparator

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel 200 milligram per square meter (mg/m²) administered IV on Day 1 of every 3 week cycle.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin Area Under the Curve (AUC)6 milligrams times minute per milliliter (mg•min/mL) administered IV on Day 1 of every 3 week cycle.

Number of subjects in period 1	Necitumumab +Paclitaxel+Carboplatin	Paclitaxel + Carboplatin
Started	110	57
Received at Least One Dose of Study Drug	106	55
Completed	93	48
Not completed	17	9
Adverse event, serious fatal	10	1
Consent withdrawn by subject	4	3
Adverse event, non-fatal	-	3
Progressive Disease	1	2
Investigator Decision	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Necitumumab +Paclitaxel+Carboplatin
Reporting group description:	
Necitumumab 800 milligram (mg) administered intravenously (IV) on Days 1 and 8 of every 3 week cycle. Paclitaxel 200 mg per square meter (mg/m²) administered IV on Day 1 of every 3 week cycle. Carboplatin AUC6 administered IV on Day 1 of every 3 week cycle.	
Reporting group title	Paclitaxel + Carboplatin
Reporting group description:	
Paclitaxel 200 mg/m² administered IV on Day 1 of every 3 week cycle. Carboplatin AUC6 administered IV on Day 1 of every 3 week cycle. The combination of paclitaxel-carboplatin may continue for a maximum of 6 cycles.	

Reporting group values	Necitumumab +Paclitaxel+Carboplatin	Paclitaxel + Carboplatin	Total
Number of subjects	110	57	167
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)	48	27	75
From 65-84 years	61	29	90
85 years and over	1	1	2
Age Continuous Units: years			
arithmetic mean	65.5	64.7	
standard deviation	± 9.36	± 8.27	-
Gender, Male/Female Units: Participants			
Female	23	13	36
Male	87	44	131
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	3	4	7
Not Hispanic or Latino	105	53	158
Unknown or Not Reported	2	0	2
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	2	2
Asian	10	6	16
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	3	2	5

White	97	47	144
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Region of Enrollment Units: Subjects			
Russian Federation	28	12	40
United States	53	25	78
Poland	12	7	19
Korea, Republic of	10	6	16
Mexico	3	3	6
Germany	4	4	8

End points

End points reporting groups

Reporting group title	Necitumumab +Paclitaxel+Carboplatin

Reporting group description:

Necitumumab 800 milligram (mg) administered intravenously (IV) on Days 1 and 8 of every 3 week cycle.
Paclitaxel 200 mg per square meter (mg/m²) administered IV on Day 1 of every 3 week cycle.
Carboplatin AUC6 administered IV on Day 1 of every 3 week cycle.

Reporting group title	Paclitaxel + Carboplatin

Reporting group description:

Paclitaxel 200 mg/m² administered IV on Day 1 of every 3 week cycle.
Carboplatin AUC6 administered IV on Day 1 of every 3 week cycle.
The combination of paclitaxel-carboplatin may continue for a maximum of 6 cycles.

Subject analysis set title	Necitumumab + Paclitaxel+ Carboplatin
Subject analysis set type	Full analysis

Subject analysis set description:

Necitumumab 800 milligram (mg) administered intravenously (IV) on Days 1 and 8 of every 3 week cycle.
Paclitaxel 200 milligram per square meter (mg/m²) administered IV on Day 1 of every 3 week cycle.
Carboplatin AUC6 administered IV on Day 1 of every 3 week cycle.

Primary: Percentage of Participants who Achieve Best Overall Tumor Response of Complete Response (CR) or Partial Response (PR) (Objective Response Rates [ORR])

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

End point description:

The denominator of ORR (Objective Response Rate) includes each participant enrolled who received any amount of study drug (necitumumab, gemcitabine, and/or cisplatin), and who had a complete radiographic assessment at baseline and at least one complete radiographic assessment post-baseline. The numerator includes those participants counted in the denominator with a confirmed best overall tumor response of partial or complete response (Complete Response (CR): disappearance of all non-nodal target lesions, with the short axes of any target lymph nodes reduced to <10 millimeters (mm). Partial Response (PR): at least a 30% decrease in the sum of the diameters of target lesions (including the short axes of any target lymph nodes), taking as reference the baseline sum diameter.) per Response Evaluation Criteria in Solid Tumors (RECIST) 1.1.

End point type	Primary

End point timeframe:

Baseline to Disease Progression or Death (Up to 24 Months)

End point values	Necitumumab +Paclitaxel+Carboplatin	Paclitaxel + Carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94[1]	50[2]		
Units: percentage of participants				
number (confidence interval 95%)	48.9 (38.5 to 59.5)	40.0 (26.4 to 54.8)		

Notes:

[1] - Participants who had study drug,1 pre and post radiographic assessment.

[2] - Participants who had study drug,1 pre and post radiographic assessment.

Statistical analyses

Statistical analysis title	Statistical Analysis Overall Response Rate

Statistical analysis description:

The denominator of ORR includes each patient randomized (for the particular treatment arm, or subgroup being analyzed) who received at least one dose of the assigned study drug and who had a complete radiographic assessment at baseline and at least one complete radiographic assessment post-baseline. The numerator includes those patients counted in the denominator with a best overall tumor response of PR or CR.

Comparison groups	Necitumumab +Paclitaxel+Carboplatin v Paclitaxel + Carboplatin
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	57.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	37.03
upper limit	57.88

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS defined as the time from the date of randomization to the date of death from any cause. For participants not known to have died as of the data cut-off date, OS was censored at the last contact date (last contact for participants in post-discontinuation = last known alive date in mortality status).

End point type	Secondary

End point timeframe:

Randomization to Date of Death (Up to 24 Months)

End point values	Necitumumab +Paclitaxel+Carboplatin	Paclitaxel + Carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110[3]	57[4]		
Units: months				
median (confidence interval 95%)	13.2 (9.7 to 15.9)	11.2 (8.2 to 12.7)		

Notes:

[3] - All randomized participants.

[4] - All randomized participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Maximum Concentration (Cmax) of Necitumumab

End point title	Pharmacokinetics (PK): Maximum Concentration (Cmax) of Necitumumab[5]

End point description:

End point type	Secondary

End point timeframe:

Pre-infusion Cycle 1, Day 1; Cycle 3, Day 1; Cycle 5; Day 1 (within 2 hours prior to beginning of infusion)

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Serum concentrations of necitumumab at each sampling time point were summarized using descriptive statistics

End point values	Necitumumab +Paclitaxel+Carboplatin			
Subject group type	Reporting group			
Number of subjects analysed	92[6]			
Units: microgram/milliliter (µg/mL)				
geometric mean (geometric coefficient of variation)				
Cycle 1, Day 1 (n=92)	262.418 (± 32.84)			
Cycle 3, Day 1 (n=72)	296.843 (± 62.97)			
Cycle 5, Day 1 (n=62)	303.475 (± 53.75)			

Notes:

[6] - All participants who received at least one dose of necitumumab and had evaluable PK data.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Anti Necitumumab Antibodies

End point title	Percentage of Participants with Anti Necitumumab Antibodies

End point description:

End point type	Secondary

End point timeframe:

Baseline to End of Cycle 6

End point values	Necitumumab + Paclitaxel+ Carboplatin			
Subject group type	Subject analysis set			
Number of subjects analysed	106[7]			
Units: percentage of participants				
number (not applicable)	2.8			

Notes:

[7] - All participants who received any amount of necitumumab and had post baseline antibody data.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival

End point title	Progression-Free Survival

End point description:

Progression-Free Survival (PFS) is defined as the time from randomization until the first radiographically documented progressive disease (PD) or death from any cause. PD defined by Response Evaluation Criteria in Solid Tumors Criteria (RECIST version 1.1) as at least a 20% increase in the sum of the diameters of target lesions,taking as reference the smallest sum on study (including the baseline sum if that is the smallest). In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. The appearance of one or more new lesions is also considered progression. For participants not known to have died as of the data cut-off date and who do not have objective PD, PFS will be censored at the date of the last complete radiographic assessment.

End point type	Secondary

End point timeframe:

Randomization to Progressive Disease or Death (Up to 24 Months)

End point values	Necitumumab +Paclitaxel+Carboplatin	Paclitaxel + Carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110[8]	57[9]		
Units: months				
median (confidence interval 95%)	5.4 (4.2 to 5.7)	5.6 (4.3 to 6.8)		

Notes:

[8] - All randomized participants.

[9] - All randomized participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieve Best Overall Disease Response of Complete Response (CR), Partial Response (PR) or Stable Disease (SD) (Disease Control Rate [DCR])

End point title	Percentage of Participants who Achieve Best Overall Disease Response of Complete Response (CR), Partial Response (PR) or Stable Disease (SD) (Disease Control Rate [DCR])

End point description:

Defined using the same denominator as defined in ORR. Among participants counted in the denominator, the numerator counts those with a confirmed best tumor response of SD, PR, or CR per RECIST 1.1. (SD: neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD; PR at least 30% decrease in the sum of diameter of target lesions; CR: disappearance of all target lesions).

End point type	Secondary

End point timeframe:

Baseline to Progressive Disease and/or Death (Estimated up to 24 Months)

End point values	Necitumumab +Paclitaxel+Carboplatin	Paclitaxel + Carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94[10]	50		
Units: percentage of participants				
number (confidence interval 95%)	87.2 (78.8 to 93.2)	84.0 (70.9 to 92.8)		

Notes:

[10] - Randomized participants who received 1 dose of study drug a complete radiographic assessment.

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Tumor Size (CTS)

End point title	Percent Change in Tumor Size (CTS)

End point description:

CTS is defined as maximum percent change from baseline in the sum of target lesions.

End point type	Secondary

End point timeframe:

Baseline to Progressive Disease or Death (Up to 24 Months)

End point values	Necitumumab +Paclitaxel+Carboplatin	Paclitaxel + Carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83[11]	43[12]		
Units: percent change in tumor size				
arithmetic mean (standard deviation)	-44.3 (± 22.8)	-38.65 (± 24.4)		

Notes:

[11] - Randomized participants who received 1 dose of study drug and had a radiographic assessment.

[12] - Randomized participants who received 1 dose of study drug and had a radiographic assessment.

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Minimum Concentration (Cmin) of Necitumumab

End point title	Pharmacokinetics (PK): Minimum Concentration (Cmin) of Necitumumab[13]

End point description:

End point type	Secondary

End point timeframe:

Cycle 1, Day 8 ; Cycle 2, Day 1; Cycle 3, Day 1;Cycle 4, Day1;Cycle 5, Day 1; Cycle 6, Day 1 (within 2 hours prior to beginning of infusion)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Serum concentrations of necitumumab at each sampling time point were summarized using descriptive statistics

End point values	Necitumumab +Paclitaxel+Carboplatin			
Subject group type	Reporting group			
Number of subjects analysed	92[14]			
Units: nanogram/milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)				
Cycle 1, Day 8 (n-85)	59.269 (± 59.06)			
Cycle 2, Day 1 (n=79)	47.874 (± 79.89)			
Cycle 3, Day 1 (n=76)	78.142 (± 70.99)			
Cycle 4, Day 1 (n=70)	80.392 (± 74.42)			
Cycle 5, Day 1 (n=62)	89.137 (± 88.94)			
Cycle 6, Day 1 (n=59)	87.043 (± 85.02)			

Notes:

[14] - Participants who received 1 dose of study drug and had evaluable PK data.

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:

I4X-MC-JFCL

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Necitumumab + Paclitaxel + Carboplatin

Reporting group description: -

Reporting group title	Paclitaxel + Carboplatin

Reporting group description: -

Serious adverse events	Necitumumab + Paclitaxel + Carboplatin	Paclitaxel + Carboplatin	
Total subjects affected by serious adverse events			
subjects affected / exposed	43 / 106 (40.57%)	21 / 55 (38.18%)	
number of deaths (all causes)	12	4	
number of deaths resulting from adverse events	3	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
malignant neoplasm progression			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
malignant pleural effusion			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
circulatory collapse			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
deep vein thrombosis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
haemorrhage			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypotension			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypovolaemic shock			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	5 / 106 (4.72%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	10 / 10	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
brain death			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
death			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 106 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
mucosal inflammation			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
non-cardiac chest pain			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
oedema peripheral			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 106 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pain			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 106 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pyrexia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	2 / 106 (1.89%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

sudden death			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 106 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
systemic inflammatory response syndrome			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 106 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
acute respiratory failure			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	2 / 106 (1.89%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
bronchial obstruction			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	2 / 106 (1.89%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
chronic obstructive pulmonary disease			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	3 / 106 (2.83%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cough			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
dyspnoea			

alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	5 / 106 (4.72%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
epistaxis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
haemoptysis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	2 / 106 (1.89%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypoxia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
interstitial lung disease			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 106 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonitis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumothorax spontaneous			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	0 / 106 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pulmonary embolism			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
pulmonary haemorrhage			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
respiratory failure			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Psychiatric disorders			
delirium			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
mental status changes			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
neutrophil count decreased			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
fall			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 106 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
thermal burn			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
atrial fibrillation			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	4 / 106 (3.77%)	4 / 55 (7.27%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
cardiac arrest			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
cardiac failure congestive			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
myocardial infarction			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	2 / 106 (1.89%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
cerebral ischaemia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 106 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
depressed level of consciousness			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
encephalopathy			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
loss of consciousness			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 106 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
neuropathy peripheral			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
syncope			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	1 / 106 (0.94%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	5 / 106 (4.72%)	4 / 55 (7.27%)	
occurrences causally related to treatment / all	3 / 5	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
anaemia of chronic disease			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
febrile neutropenia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	7 / 106 (6.60%)	2 / 55 (3.64%)	
occurrences causally related to treatment / all	5 / 7	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
leukopenia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	2 / 106 (1.89%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
neutropenia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	5 / 106 (4.72%)	2 / 55 (3.64%)	
occurrences causally related to treatment / all	3 / 5	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
thrombocytopenia			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	2 / 106 (1.89%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
constipation			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 106 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
diarrhoea			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
dysphagia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastric ulcer haemorrhage			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastrooesophageal reflux disease			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ileus			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
small intestinal obstruction			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
stomatitis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
upper gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
vomiting			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 106 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	2 / 106 (1.89%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
muscular weakness			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 106 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
bacterial sepsis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
cellulitis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
clostridium difficile colitis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	2 / 106 (1.89%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
diverticulitis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
herpes simplex			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
herpes zoster			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 106 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
lung infection			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
perirectal abscess			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 106 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	14 / 106 (13.21%)	4 / 55 (7.27%)	
occurrences causally related to treatment / all	3 / 15	1 / 4	
deaths causally related to treatment / all	0 / 1	0 / 1	
pneumonia bacterial			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 106 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia viral			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

sepsis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	3 / 106 (2.83%)	2 / 55 (3.64%)	
occurrences causally related to treatment / all	4 / 4	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
septic shock			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
urinary tract infection			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (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			
dehydration			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	3 / 106 (2.83%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	2 / 3	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypocalcaemia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypomagnesaemia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Necitumumab + Paclitaxel + Carboplatin	Paclitaxel + Carboplatin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	102 / 106 (96.23%)	49 / 55 (89.09%)	
Vascular disorders			
hypotension			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	12 / 106 (11.32%)	7 / 55 (12.73%)	
occurrences (all)	13	10	
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	18 / 106 (16.98%)	3 / 55 (5.45%)	
occurrences (all)	31	5	
fatigue			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	33 / 106 (31.13%)	24 / 55 (43.64%)	
occurrences (all)	52	48	
non-cardiac chest pain			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	7 / 106 (6.60%)	1 / 55 (1.82%)	
occurrences (all)	8	1	
oedema peripheral			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	11 / 106 (10.38%)	7 / 55 (12.73%)	
occurrences (all)	15	9	
pain			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	7 / 106 (6.60%)	0 / 55 (0.00%)	
occurrences (all)	9	0	
pyrexia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	10 / 106 (9.43%)	4 / 55 (7.27%)	
occurrences (all)	16	5	
Respiratory, thoracic and mediastinal			

disorders				
cough				
alternative dictionary used: MedDRA 20.0				
subjects affected / exposed	18 / 106 (16.98%)	10 / 55 (18.18%)		
occurrences (all)	24	10		
dysphonia				
alternative dictionary used: MedDRA 20.0				
subjects affected / exposed	4 / 106 (3.77%)	3 / 55 (5.45%)		
occurrences (all)	5	4		
dyspnoea				
alternative dictionary used: MedDRA 20.0				
subjects affected / exposed	23 / 106 (21.70%)	6 / 55 (10.91%)		
occurrences (all)	29	13		
dyspnoea exertional				
alternative dictionary used: MedDRA 20.0				
subjects affected / exposed	0 / 106 (0.00%)	3 / 55 (5.45%)		
occurrences (all)	0	4		
epistaxis				
alternative dictionary used: MedDRA 20.0				
subjects affected / exposed	2 / 106 (1.89%)	3 / 55 (5.45%)		
occurrences (all)	2	3		
haemoptysis				
alternative dictionary used: MedDRA 20.0				
subjects affected / exposed	7 / 106 (6.60%)	6 / 55 (10.91%)		
occurrences (all)	7	8		
nasal congestion				
alternative dictionary used: MedDRA 20.0				
subjects affected / exposed	4 / 106 (3.77%)	3 / 55 (5.45%)		
occurrences (all)	6	3		
oropharyngeal pain				
alternative dictionary used: MedDRA 20.0				
subjects affected / exposed	3 / 106 (2.83%)	3 / 55 (5.45%)		
occurrences (all)	3	3		
productive cough				
alternative dictionary used: MedDRA 20.0				

subjects affected / exposed	1 / 106 (0.94%)	3 / 55 (5.45%)	
occurrences (all)	1	4	
Psychiatric disorders			
anxiety			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	6 / 106 (5.66%)	0 / 55 (0.00%)	
occurrences (all)	6	0	
insomnia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	14 / 106 (13.21%)	6 / 55 (10.91%)	
occurrences (all)	16	7	
Investigations			
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	7 / 106 (6.60%)	0 / 55 (0.00%)	
occurrences (all)	9	0	
neutrophil count decreased			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	8 / 106 (7.55%)	6 / 55 (10.91%)	
occurrences (all)	18	7	
weight decreased			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	31 / 106 (29.25%)	14 / 55 (25.45%)	
occurrences (all)	49	20	
Injury, poisoning and procedural complications			
fall			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	2 / 106 (1.89%)	3 / 55 (5.45%)	
occurrences (all)	2	4	
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	14 / 106 (13.21%)	8 / 55 (14.55%)	
occurrences (all)	16	10	
dysgeusia			

alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	8 / 106 (7.55%)	4 / 55 (7.27%)	
occurrences (all)	10	4	
headache			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	4 / 106 (3.77%)	7 / 55 (12.73%)	
occurrences (all)	6	7	
neuropathy peripheral			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	13 / 106 (12.26%)	9 / 55 (16.36%)	
occurrences (all)	21	18	
paraesthesia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	3 / 106 (2.83%)	3 / 55 (5.45%)	
occurrences (all)	3	3	
peripheral sensory neuropathy			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	31 / 106 (29.25%)	13 / 55 (23.64%)	
occurrences (all)	54	24	
syncope			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	8 / 106 (7.55%)	1 / 55 (1.82%)	
occurrences (all)	8	1	
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	34 / 106 (32.08%)	27 / 55 (49.09%)	
occurrences (all)	87	62	
leukopenia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	9 / 106 (8.49%)	9 / 55 (16.36%)	
occurrences (all)	16	15	
neutropenia			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	37 / 106 (34.91%)	16 / 55 (29.09%)	
occurrences (all)	73	43	
thrombocytopenia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	27 / 106 (25.47%)	14 / 55 (25.45%)	
occurrences (all)	67	31	
Eye disorders			
vision blurred			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	2 / 106 (1.89%)	3 / 55 (5.45%)	
occurrences (all)	2	3	
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	8 / 106 (7.55%)	2 / 55 (3.64%)	
occurrences (all)	11	2	
constipation			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	25 / 106 (23.58%)	15 / 55 (27.27%)	
occurrences (all)	28	23	
diarrhoea			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	26 / 106 (24.53%)	12 / 55 (21.82%)	
occurrences (all)	34	18	
dyspepsia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	6 / 106 (5.66%)	3 / 55 (5.45%)	
occurrences (all)	6	3	
nausea			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	27 / 106 (25.47%)	20 / 55 (36.36%)	
occurrences (all)	35	34	
stomatitis			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	14 / 106 (13.21%)	3 / 55 (5.45%)	
occurrences (all)	15	3	
vomiting			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	13 / 106 (12.26%)	8 / 55 (14.55%)	
occurrences (all)	17	11	
Skin and subcutaneous tissue disorders			
alopecia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	28 / 106 (26.42%)	10 / 55 (18.18%)	
occurrences (all)	30	11	
dermatitis acneiform			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	23 / 106 (21.70%)	0 / 55 (0.00%)	
occurrences (all)	40	0	
dry skin			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	13 / 106 (12.26%)	1 / 55 (1.82%)	
occurrences (all)	13	1	
pruritus			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	6 / 106 (5.66%)	0 / 55 (0.00%)	
occurrences (all)	6	0	
rash			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	22 / 106 (20.75%)	1 / 55 (1.82%)	
occurrences (all)	69	1	
rash maculo-papular			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	8 / 106 (7.55%)	0 / 55 (0.00%)	
occurrences (all)	17	0	
rash papular			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	12 / 106 (11.32%)	0 / 55 (0.00%)	
occurrences (all)	16	0	
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	24 / 106 (22.64%)	13 / 55 (23.64%)	
occurrences (all)	61	29	
back pain			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	10 / 106 (9.43%)	3 / 55 (5.45%)	
occurrences (all)	11	3	
bone pain			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	8 / 106 (7.55%)	8 / 55 (14.55%)	
occurrences (all)	10	14	
muscular weakness			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	10 / 106 (9.43%)	4 / 55 (7.27%)	
occurrences (all)	10	7	
musculoskeletal chest pain			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 106 (0.94%)	7 / 55 (12.73%)	
occurrences (all)	1	9	
musculoskeletal pain			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	3 / 106 (2.83%)	4 / 55 (7.27%)	
occurrences (all)	5	7	
myalgia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	18 / 106 (16.98%)	12 / 55 (21.82%)	
occurrences (all)	44	21	
pain in extremity			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	8 / 106 (7.55%)	8 / 55 (14.55%)	
occurrences (all)	10	8	
Infections and infestations			
conjunctivitis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	7 / 106 (6.60%)	0 / 55 (0.00%)	
occurrences (all)	9	0	
paronychia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	6 / 106 (5.66%)	0 / 55 (0.00%)	
occurrences (all)	9	0	
pneumonia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	6 / 106 (5.66%)	2 / 55 (3.64%)	
occurrences (all)	9	2	
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	34 / 106 (32.08%)	15 / 55 (27.27%)	
occurrences (all)	40	20	
dehydration			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	11 / 106 (10.38%)	10 / 55 (18.18%)	
occurrences (all)	15	17	
hypoalbuminaemia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	5 / 106 (4.72%)	3 / 55 (5.45%)	
occurrences (all)	9	4	
hypocalcaemia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	10 / 106 (9.43%)	2 / 55 (3.64%)	
occurrences (all)	19	2	
hypokalaemia			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	14 / 106 (13.21%)	4 / 55 (7.27%)	
occurrences (all)	28	7	
hypomagnesaemia alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	25 / 106 (23.58%)	7 / 55 (12.73%)	
occurrences (all)	74	12	
hyponatraemia alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	7 / 106 (6.60%)	1 / 55 (1.82%)	
occurrences (all)	13	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported