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

Summary

EudraCT number	2012-003201-96
Trial protocol	NL ES
Global end of trial date	03 December 2015

Results information

Result version number	v1 (current)
This version publication date	07 August 2016
First version publication date	07 August 2016

Trial information

Trial identification

Sponsor protocol code	14789

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01788566
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Alias: I4X-MC-JFCK, Trial Number: 14789

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877-CTLilly,
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877-285-4559,

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 December 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to see how participants with late stage lung cancer do on gemcitabine-cisplatin chemotherapy plus necitumumab. The study will also see how safe the drugs are in combination and to see how long the medicine stays in the body. The study will last approximately 2 years.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 March 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	United States: 11
Country: Number of subjects enrolled	Taiwan: 8
Country: Number of subjects enrolled	Mexico: 1
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Spain: 25
Country: Number of subjects enrolled	Korea, Republic of: 3
Worldwide total number of subjects	61
EEA total number of subjects	33

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)	28
From 65 to 84 years	33
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	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Gemcitabine + Cisplatin + Necitumumab

Arm description:

Necitumumab administered intravenously (IV) 800 milligram (mg) on Days 1 and 8 of each 3-week cycle.
Gemcitabine administered IV at 1250 milligram per square meter (mg/m^2) on Days 1 and 8 of each 3 week cycle for a maximum of 6 cycles.
Cisplatin administered IV at 75 mg/m^2 on Day 1 of each 3 week cycle for a maximum of 6 cycles.

Arm type	Experimental
Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	Gemzar®, LY188011
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine administered IV at 1250 milligram per square meter (mg/m^2) on Days 1 and 8 of each 3 week cycle for a maximum of 6 cycles.

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatin administered IV at 75 mg/m^2 on Day 1 of each 3 week cycle for a maximum of 6 cycles.

Investigational medicinal product name	Necitumumab
Investigational medicinal product code	
Other name	IMC-1IF8, LY3012211, Portrazza®
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

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

Number of subjects in period 1	Gemcitabine + Cisplatin + Necitumumab
Started	61
Completed	53
Not completed	8
Adverse event, serious fatal	4
Clinical Progressive Disease	3
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups	
Reporting group title	Gemcitabine + Cisplatin + Necitumumab
Reporting group description:	
Necitumumab administered intravenously (IV) 800 milligram (mg) on Days 1 and 8 of each 3-week cycle. Gemcitabine administered IV at 1250 milligram per square meter (mg/m^2) on Days 1 and 8 of each 3 week cycle for a maximum of 6 cycles. Cisplatin administered IV at 75 mg/m^2 on Day 1 of each 3 week cycle for a maximum of 6 cycles.	

Reporting group values	Gemcitabine + Cisplatin + Necitumumab	Total	
Number of subjects	61	61	
Age Categorical Units: participants			
<=18 years	0	0	
Between 18 and 65 years	28	28	
>=65 years	33	33	
Gender, Male/Female Units: participants			
Female	12	12	
Male	49	49	
Race/Ethnicity, Customized Units: Subjects			
White	48	48	
Asian	11	11	
Black or African American	1	1	
Missing	1	1	
Region of Enrollment Units: Subjects			
Canada	5	5	
Netherlands	5	5	
United States	11	11	
Taiwan	8	8	
Mexico	1	1	
France	3	3	
Spain	25	25	
Korea, Republic of	3	3	

End points

End points reporting groups

Reporting group title	Gemcitabine + Cisplatin + Necitumumab

Reporting group description:

Necitumumab administered intravenously (IV) 800 milligram (mg) on Days 1 and 8 of each 3-week cycle.
Gemcitabine administered IV at 1250 milligram per square meter (mg/m^2) on Days 1 and 8 of each 3 week cycle for a maximum of 6 cycles.
Cisplatin administered IV at 75 mg/m^2 on Day 1 of each 3 week cycle for a maximum of 6 cycles.

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

End point title	Percentage of Participants who Achieve Best Overall Tumor Response of Complete Response (CR) or Partial Response (PR) Objective Tumor Response Rate (ORR)[1]

End point description:

ORR is confirmed best overall tumor response of CR or PR. According to RECIST v1.1, PR defined as a >30% decrease in the sum of the longest diameters (LD) of the target lesions, taking as reference the baseline sum of the LD; CR was defined as the disappearance of all target and non-target lesions. Percentage of participants was calculated as: total number of participants with a best tumor response of PR or CR among participants counted in the denominator/total number of participants treated with any amount of study drug, who has a complete radiographic assessment at baseline, and who has at least 1 complete radiographic assessment at postbaseline x 100%.

End point type	Primary

End point timeframe:

Baseline to Measured Progressive Disease (up to 17 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: The ORR and its Exact 95% confidence intervals were estimated.

End point values	Gemcitabine + Cisplatin + Necitumumab			
Subject group type	Reporting group			
Number of subjects analysed	54[2]			
Units: Percentage of participants				
number (confidence interval 95%)	48.1 (34.34 to 62.16)			

Notes:

[2] - All participants who received any amount of study treatment and had evaluable radiographic data.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Overall survival (OS) duration is defined from the date of first dose of study drug to the date of death from any cause. OS was estimated by the Kaplan-Meier method. For participants who were not known to

have died as of the data cut-off date, OS was censored at the date of last contact prior to the data cutoff date.

End point type	Secondary

End point timeframe:

Baseline to Death from Any Cause (up to 17 Months)

End point values	Gemcitabine + Cisplatin + Necitumumab			
Subject group type	Reporting group			
Number of subjects analysed	61[3]			
Units: months				
median (confidence interval 95%)	11.7 (7.59 to 99999)			

Notes:

[3] - The 95% confidence interval upper limit was not calculable due to the censored data at data cutoff.

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 defined as the time from the date of first dose of study drug until objective progressive disease (PD) or death for any cause. According to Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1), PD was at least a 20% increase in the sum of the diameters of target lesions, taking as reference the smallest sum on study. In addition to the 20% relative increase, the sum must have also demonstrated an absolute increase of at least 5 millimeters (mm). The appearance of 1 or more new lesions was 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:

Baseline to Measured Progressive Disease or Death from Any Cause (up to 17 Months)

End point values	Gemcitabine + Cisplatin + Necitumumab			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: months				
median (confidence interval 95%)	5.6 (3.68 to 6.87)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number 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	Number 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:

DCR is best overall response of SD, PR or CR. According to RECIST v1.1, PR defined as a ≥30% decrease in the sum of the longest diameters (LD) of the target lesions, taking as reference the baseline sum of the LD; CR was defined as the disappearance of all target and non-target lesions. SD was neither sufficient shrinkage to qualify as PR nor sufficient increase to qualify as PD, taking as reference the smallest sum diameter since treatment started. Percentage of participants who achieved disease control = (those participants counted in the denominator with a best tumor response of SD, PR, or CR)/(the same denominator as for ORR)*100.

End point type	Secondary

End point timeframe:

Baseline to Measured Progressive Disease or Participants Stops Study (up to 17 Months)

End point values	Gemcitabine + Cisplatin + Necitumumab			
Subject group type	Reporting group			
Number of subjects analysed	54[4]			
Units: percentage of participants				
number (confidence interval 95%)	81.5 (68.57 to 90.75)			

Notes:

[4] - All participants who received any amount of study treatment and had evaluable radiographic data.

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 improvement from baseline in the sum of target lesions.

End point type	Secondary

End point timeframe:

Baseline until Measured Progressive Disease (up to 17 Months)

End point values	Gemcitabine + Cisplatin + Necitumumab			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: percent change				
arithmetic mean (standard deviation)	39.68 (± 21.296)			

Statistical analyses

No statistical analyses for this end point

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

End point title	Pharmacokinetics (PK): Minimum (Cmin) Maximum Concentration (Cmax) of Necitumumab

End point description:

Pre-infusion Minimum Concentration (Cmin) and post-infusion (Cmax) necitumumab serum concentration

End point type	Secondary

End point timeframe:

Predose Cycle 1 Day 8; Cycle 2 through 6 Day 1; End of Infusion (EOI) Cycle 1, 3, 5 Day 1

End point values	Gemcitabine + Cisplatin + Necitumumab			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: micrograms/milliliter (ug/ml)				
geometric mean (geometric coefficient of variation)				
Predose Cycle 1 Day 8	70.8 (± 36.7)			
Predose Cycle 2 Day 1	67.5 (± 78)			
Predose Cycle 3 Day 1	106 (± 36.6)			
Predose Cycle 4 Day 1	115 (± 43.9)			
Predose Cycle 5 Day 1	141 (± 62.3)			
Predose Cycle 6 Day 1	126 (± 34.2)			
EOI Cycle 1 Day 1	266 (± 24.8)			
EOI Cycle 3 Day 1	352 (± 29.5)			
EOI Cycle 5 Day 1	360 (± 29.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Anti-Necitumumab Antibodies

End point title	Number of Participants with Anti-Necitumumab Antibodies

End point description:

A participant was considered to have an anti-necitumumab antibody response if anti-drug antibodies (ADA) were detected at any time point. Treatment emergent antibodies were defined as any anti-necitumumab antibody titer equal to or greater than 4-fold the participant's baseline titer.

End point type	Secondary

End point timeframe:

Baseline up to 30 Days Post Last Infusion (up to 17 Months)

End point values	Gemcitabine + Cisplatin + Necitumumab			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: participants				
number (not applicable)				
Number of Participants with 1 Positive Titer	9			
Treatment Emergent Antibody Positive	4			
Neutralizing Antibody Detected	3			

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-JFCK

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Necitumumab + Gemcitabine + Cisplatin

Reporting group description: -

Serious adverse events	Necitumumab + Gemcitabine + Cisplatin		
Total subjects affected by serious adverse events			
subjects affected / exposed	33 / 61 (54.10%)		
number of deaths (all causes)	7		
number of deaths resulting from adverse events	2		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
malignant neoplasm progression			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
tumour associated fever			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
aortic thrombosis			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
orthostatic hypotension				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
superior vena cava syndrome				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
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 16.0				
subjects affected / exposed	2 / 61 (3.28%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	1 / 1			
fatigue				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	2 / 61 (3.28%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
malaise				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	2 / 61 (3.28%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 1			
pyrexia				
alternative dictionary used: MedDRA 16.0				

subjects affected / exposed	2 / 61 (3.28%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
acute interstitial pneumonitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
acute respiratory failure			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
atelectasis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
chronic obstructive pulmonary disease			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
dyspnoea			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
haemoptysis			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
pulmonary embolism				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
pulmonary haemorrhage				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
respiratory distress				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Psychiatric disorders				
anxiety				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
confusional state				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
conduct disorder				
alternative dictionary used: MedDRA 16.0				

subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
accidental overdose			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
pulmonary radiation injury			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
atrial fibrillation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
cardiac tamponade			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
myocardial infarction			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
ischaemic stroke			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
febrile neutropenia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	3 / 61 (4.92%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
diarrhoea			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
duodenal perforation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
enteritis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
gastric perforation			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
intestinal ischaemia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
stomatitis				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
haematuria				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
flank pain				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
bronchitis				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
catheter site abscess				
alternative dictionary used: MedDRA 16.0				

subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
clostridium difficile infection			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
diverticulitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
neutropenic sepsis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
pneumonia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	4 / 61 (6.56%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
pneumonia haemophilus			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
pseudomembranous colitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

respiratory tract infection				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	2 / 61 (3.28%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
sepsis				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
upper respiratory tract infection				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
urosepsis				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
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 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
dehydration				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
hypercalcaemia				
alternative dictionary used: MedDRA 16.0				

subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
hypomagnesaemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
hyponatraemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Necitumumab + Gemcitabine + Cisplatin		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	61 / 61 (100.00%)		
Vascular disorders			
aortic thrombosis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
embolism			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences (all)	2		
haematoma			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
hypertension			
alternative dictionary used:			

MedDRA 16.0				
subjects affected / exposed	5 / 61 (8.20%)			
occurrences (all)	5			
hypotension				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	3 / 61 (4.92%)			
occurrences (all)	3			
jugular vein distension				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
jugular vein thrombosis				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	2 / 61 (3.28%)			
occurrences (all)	2			
orthostatic hypotension				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	2 / 61 (3.28%)			
occurrences (all)	2			
peripheral artery thrombosis				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
peripheral venous disease				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
raynaud's phenomenon				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
superior vena cava syndrome				
alternative dictionary used: MedDRA 16.0				

subjects affected / exposed	2 / 61 (3.28%)		
occurrences (all)	2		
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	25 / 61 (40.98%)		
occurrences (all)	83		
axillary pain			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
chest pain			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
chills			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	3 / 61 (4.92%)		
occurrences (all)	3		
face oedema			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences (all)	2		
fatigue			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	22 / 61 (36.07%)		
occurrences (all)	39		
feeling cold			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences (all)	2		
gait disturbance			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	3 / 61 (4.92%)			
occurrences (all)	3			
general physical health deterioration				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
influenza like illness				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	2 / 61 (3.28%)			
occurrences (all)	2			
infusion site extravasation				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
infusion site pain				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	2 / 61 (3.28%)			
occurrences (all)	2			
infusion site urticaria				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
malaise				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	5 / 61 (8.20%)			
occurrences (all)	5			
mucosal dryness				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	2 / 61 (3.28%)			
occurrences (all)	4			
mucosal inflammation				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	7 / 61 (11.48%)			
occurrences (all)	9			

non-cardiac chest pain			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	4 / 61 (6.56%)		
occurrences (all)	8		
oedema			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
oedema peripheral			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	6 / 61 (9.84%)		
occurrences (all)	7		
pain			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences (all)	2		
pyrexia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	12 / 61 (19.67%)		
occurrences (all)	17		
Immune system disorders			
hypersensitivity			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Reproductive system and breast disorders			
benign prostatic hyperplasia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed[1]	1 / 49 (2.04%)		
occurrences (all)	1		
testicular pain			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed[2]	1 / 49 (2.04%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal			

disorders				
acute interstitial pneumonitis				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
atelectasis				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
bronchospasm				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
catarrh				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	3 / 61 (4.92%)			
occurrences (all)	4			
chronic obstructive pulmonary disease				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
cough				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	17 / 61 (27.87%)			
occurrences (all)	24			
dysphonia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	2 / 61 (3.28%)			
occurrences (all)	2			
dyspnoea				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	16 / 61 (26.23%)			
occurrences (all)	23			
epistaxis				
alternative dictionary used:				

MedDRA 16.0				
subjects affected / exposed	7 / 61 (11.48%)			
occurrences (all)	8			
haemoptysis				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	6 / 61 (9.84%)			
occurrences (all)	12			
hiccups				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	5 / 61 (8.20%)			
occurrences (all)	5			
nasal congestion				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
nasal dryness				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
oropharyngeal discomfort				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
pleural effusion				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
pleuritic pain				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	2			
productive cough				
alternative dictionary used: MedDRA 16.0				

subjects affected / exposed	9 / 61 (14.75%)		
occurrences (all)	14		
pulmonary embolism			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	3 / 61 (4.92%)		
occurrences (all)	3		
rhinorrhoea			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	3 / 61 (4.92%)		
occurrences (all)	3		
Psychiatric disorders			
anxiety			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	4 / 61 (6.56%)		
occurrences (all)	4		
confusional state			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences (all)	2		
delirium			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
depression			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences (all)	2		
insomnia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	12 / 61 (19.67%)		
occurrences (all)	14		
irritability			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences (all)	2		
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
blood alkaline phosphatase increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
blood bilirubin increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
blood creatinine increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences (all)	2		
blood urea increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
fibrin d dimer increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
glomerular filtration rate increased			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
haemoglobin decreased				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
lymphocyte count decreased				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
lymphocyte count increased				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
neutrophil count decreased				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	5 / 61 (8.20%)			
occurrences (all)	11			
platelet count decreased				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	5 / 61 (8.20%)			
occurrences (all)	11			
platelet count increased				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	3 / 61 (4.92%)			
occurrences (all)	3			
respiratory rate increased				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
troponin i increased				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			

weight decreased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	18 / 61 (29.51%)		
occurrences (all)	24		
weight increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	5 / 61 (8.20%)		
occurrences (all)	5		
white blood cell count decreased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	3 / 61 (4.92%)		
occurrences (all)	3		
Injury, poisoning and procedural complications			
fall			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences (all)	2		
fracture			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
infusion related reaction			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences (all)	2		
Cardiac disorders			
myocardial ischaemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
palpitations			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
sinus tachycardia			

alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
tachycardia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	2 / 61 (3.28%)			
occurrences (all)	2			
Nervous system disorders				
aphasia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
aphonia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
ataxia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
cerebrovascular accident				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
dizziness				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	14 / 61 (22.95%)			
occurrences (all)	17			
dysaesthesia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
dysarthria				
alternative dictionary used: MedDRA 16.0				

subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
dysgeusia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	8 / 61 (13.11%)			
occurrences (all)	8			
headache				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	10 / 61 (16.39%)			
occurrences (all)	12			
ischaemic stroke				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
lethargy				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	2 / 61 (3.28%)			
occurrences (all)	2			
neuralgia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
neuropathy peripheral				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	4 / 61 (6.56%)			
occurrences (all)	10			
neurotoxicity				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	4 / 61 (6.56%)			
occurrences (all)	4			
paraesthesia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	5 / 61 (8.20%)			
occurrences (all)	8			

peripheral motor neuropathy				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	3 / 61 (4.92%)			
occurrences (all)	4			
peripheral sensory neuropathy				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
syncope				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	3 / 61 (4.92%)			
occurrences (all)	3			
tremor				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
Blood and lymphatic system disorders				
anaemia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	15 / 61 (24.59%)			
occurrences (all)	38			
iron deficiency anaemia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
leukopenia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	3 / 61 (4.92%)			
occurrences (all)	6			
neutropenia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	19 / 61 (31.15%)			
occurrences (all)	51			
thrombocytopenia				
alternative dictionary used: MedDRA 16.0				

subjects affected / exposed	10 / 61 (16.39%)		
occurrences (all)	20		
Ear and labyrinth disorders			
deafness			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
hearing impaired			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences (all)	2		
hypoacusis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
ototoxicity			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	7 / 61 (11.48%)		
occurrences (all)	14		
tinnitus			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	4 / 61 (6.56%)		
occurrences (all)	4		
vertigo			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Eye disorders			
blepharitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
cataract			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
dry eye				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	3 / 61 (4.92%)			
occurrences (all)	3			
growth of eyelashes				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
lacrimation increased				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
visual acuity reduced				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	2 / 61 (3.28%)			
occurrences (all)	2			
Gastrointestinal disorders				
abdominal distension				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	3 / 61 (4.92%)			
occurrences (all)	3			
abdominal pain				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	8 / 61 (13.11%)			
occurrences (all)	10			
abdominal pain upper				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	5 / 61 (8.20%)			
occurrences (all)	5			
cheilitis				
alternative dictionary used: MedDRA 16.0				

subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	2			
constipation				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	20 / 61 (32.79%)			
occurrences (all)	25			
diarrhoea				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	18 / 61 (29.51%)			
occurrences (all)	29			
dry mouth				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
dyspepsia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	3 / 61 (4.92%)			
occurrences (all)	6			
dysphagia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	7 / 61 (11.48%)			
occurrences (all)	7			
gastrointestinal pain				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
gastrooesophageal reflux disease				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	2 / 61 (3.28%)			
occurrences (all)	2			
lip dry				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			

lower gastrointestinal haemorrhage				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
mouth ulceration				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	2 / 61 (3.28%)			
occurrences (all)	2			
nausea				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	45 / 61 (73.77%)			
occurrences (all)	79			
odynophagia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	2 / 61 (3.28%)			
occurrences (all)	2			
oesophageal pain				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
oesophagitis				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
rectal haemorrhage				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
retching				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
stomatitis				
alternative dictionary used: MedDRA 16.0				

subjects affected / exposed	21 / 61 (34.43%)		
occurrences (all)	44		
vomiting			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	22 / 61 (36.07%)		
occurrences (all)	39		
Skin and subcutaneous tissue disorders			
acne			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences (all)	2		
alopecia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	9 / 61 (14.75%)		
occurrences (all)	10		
decubitus ulcer			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
dermatitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
dermatitis acneiform			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	12 / 61 (19.67%)		
occurrences (all)	17		
dry skin			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	12 / 61 (19.67%)		
occurrences (all)	25		
erythema			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
hair colour changes				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
hair disorder				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
hirsutism				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed[3]	1 / 12 (8.33%)			
occurrences (all)	1			
hypertrichosis				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
nail dystrophy				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
onycholysis				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	2 / 61 (3.28%)			
occurrences (all)	2			
pain of skin				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
palmar-plantar erythrodysaesthesia syndrome				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	2			

penile ulceration				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed[4]	1 / 49 (2.04%)			
occurrences (all)	1			
pruritus				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	5 / 61 (8.20%)			
occurrences (all)	6			
rash				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	28 / 61 (45.90%)			
occurrences (all)	109			
rash generalised				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
rash maculo-papular				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	4 / 61 (6.56%)			
occurrences (all)	5			
rash vesicular				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
scab				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
skin fissures				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	8 / 61 (13.11%)			
occurrences (all)	15			
skin toxicity				
alternative dictionary used: MedDRA 16.0				

subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
skin ulcer			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	2		
urticaria			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	11		
xeroderma			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences (all)	2		
cystitis noninfective			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
dysuria			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	3 / 61 (4.92%)		
occurrences (all)	3		
haematuria			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences (all)	2		
micturition frequency decreased			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
proteinuria			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	3 / 61 (4.92%)		
occurrences (all)	3		
urinary incontinence			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
urinary retention			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	5 / 61 (8.20%)		
occurrences (all)	6		
arthritis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
back pain			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	4 / 61 (6.56%)		
occurrences (all)	6		
flank pain			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	3 / 61 (4.92%)		
occurrences (all)	3		
groin pain			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
muscle spasms			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
muscular weakness			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	5 / 61 (8.20%)		
occurrences (all)	5		
musculoskeletal chest pain			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	3 / 61 (4.92%)		
occurrences (all)	3		
musculoskeletal pain			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	3 / 61 (4.92%)		
occurrences (all)	3		
myalgia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
neck pain			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
pain in extremity			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	7 / 61 (11.48%)		
occurrences (all)	7		
Infections and infestations			
adenoviral conjunctivitis			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
bronchitis				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
candida infection				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
clostridium difficile infection				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	2			
conjunctivitis				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	6 / 61 (9.84%)			
occurrences (all)	11			
dermatophytosis of nail				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
device related infection				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
folliculitis				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
gastroenteritis				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	3 / 61 (4.92%)			
occurrences (all)	3			

genital infection fungal				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
herpes virus infection				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
impetigo				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
influenza				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	2			
nail infection				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	2 / 61 (3.28%)			
occurrences (all)	4			
nasopharyngitis				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	2 / 61 (3.28%)			
occurrences (all)	2			
oral candidiasis				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
paronychia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	12 / 61 (19.67%)			
occurrences (all)	40			
pharyngitis				
alternative dictionary used: MedDRA 16.0				

subjects affected / exposed	2 / 61 (3.28%)			
occurrences (all)	2			
pneumonia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
respiratory tract infection				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	3 / 61 (4.92%)			
occurrences (all)	3			
rhinitis				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
scrotal infection				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed[5]	1 / 49 (2.04%)			
occurrences (all)	1			
skin infection				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	2 / 61 (3.28%)			
occurrences (all)	3			
soft tissue infection				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
upper respiratory tract infection				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences (all)	1			
urinary tract infection				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	6 / 61 (9.84%)			
occurrences (all)	6			

viral infection			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
wound infection			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
cachexia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
decreased appetite			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	35 / 61 (57.38%)		
occurrences (all)	52		
dehydration			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	5 / 61 (8.20%)		
occurrences (all)	8		
hypercalcaemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
hyperglycaemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences (all)	5		
hyperkalaemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	3 / 61 (4.92%)		
occurrences (all)	4		
hypermagnesaemia			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
hypernatraemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
hypoalbuminaemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences (all)	2		
hypocalcaemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences (all)	11		
hypokalaemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	8 / 61 (13.11%)		
occurrences (all)	19		
hypomagnesaemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	20 / 61 (32.79%)		
occurrences (all)	45		
hyponatraemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences (all)	3		
hypophosphataemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		

Notes:

[1] - 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.

[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.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 September 2012	I4X-MC-JFCK(a) Reduced patients number, removed control arm, disconnected from JFCL.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported