



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
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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
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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/m²) on Days 1 and 8 of each 3 week cycle for a maximum of 6 cycles.

Cisplatin administered IV at 75 mg/m² 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/m²) 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/m² 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
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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/m²) on Days 1 and 8 of each 3 week cycle for a maximum of 6 cycles.

Cisplatin administered IV at 75 mg/m² 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]
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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
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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)
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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
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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)
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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
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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)]
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End point description:

DCR is best overall response of SD, PR or CR. According to RECIST v1.1, PR defined as a $\geq 30\%$ 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
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End point timeframe:

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

End point values	Gemcitabine + Cisplatin + Nectinumab			
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)
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End point description:

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

End point type	Secondary
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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
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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
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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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.0
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Reporting groups

Reporting group title	Necitumumab + Gemcitabine + Cisplatin
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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		

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

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

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		

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

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

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		

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

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

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

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			

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

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 erythrodysesthesia 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			

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

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

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		

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

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