Clinical trial results:
Phase I/II study of continous infusion with 5-FU and weekly Oxaliplatin / Cetuximab combined with concurrent radiation as neoadjuvant treatment in locally advanced oesophageal squamous cell carcinoma.

Summary

EudraCT number	2006-001097-24
Trial protocol	DE
Global end of trial date	13 August 2015

Results information

Result version number	v1 (current)
This version publication date	16 December 2020
First version publication date	16 December 2020

Trial information

Trial identification

Sponsor protocol code	OE7-432-LOR-0033-I

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00425425
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Technische Universität München, Fakultät für Medizin
Sponsor organisation address	Ismaninger Str. 22, München, Germany, 81675
Public contact	Sandra Eckert , Klinikum rechts der Isar Klinik und Poliklinik, Studiensekretariat , 49 89 4140 5736111,
Scientific contact	Klinik und Poliklinik für Innere Medizin III, Technische Universität München, Fakultät für Medizin, Klinikum rechts der Isar, 49 89 4140 4111,

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	24 June 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 August 2015
Global end of trial reached?	Yes
Global end of trial date	13 August 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This phase I/II trial is studying the side effects and best dose of oxaliplatin and fluorouracil when given together with cetuximab and radiation therapy and to see how well they work in treating patients with stage II or stage III esophageal cancer.
Definition of the maximal tolerated dose for the combination of Cetuximab plus Oxaliplatin combined with concurrent radiation as neoadjuvant treatment.

Primary
•Determine the maximum tolerated dose of oxaliplatin and fluorouracil when administered with cetuximab and radiotherapy in patients with stage II or III squamous cell carcinoma of the esophagus. (Phase I)
•Determine the response rate in patients treated with this regimen. (Phase II)

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance the ethical principles of Good Clinical Practice (GCP).
Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision.
The study was regularly monitored by the Sponsor and all investigators connected to the study were GCP trained.

Background therapy:

Standard of care.
Concomitant medication and supportive therapy were carried out according to standard clinical guidelines and at the judgement of the investigators.
For a maximum of six 29-day cycles, patients received cisplatin (IMP No. 1) 100 mg/m2, day 1, plus 5-FU 1000 mg/m2, days 1–5 (CF), either alone or in combination with cetuximab (IMP No. 2) (CET–CF; 400 mg/m2 initial dose followed by 250 mg/m2 weekly thereafter).

So all patient recieved for a maximum of six 29-day cycles, 5-FU 1000 mg/m2, days 1–5 (CF).

Evidence for comparator: -

Actual start date of recruitment	28 September 2006
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Scientific research
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 35
Worldwide total number of subjects	35
EEA total number of subjects	35

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	26
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted multicentric in Germany between 28.09.2006 (first patient in) and 06.05.2010 (last patient completed).

Pre-assignment

Screening details:

Patients must have all screening evaluations performed prior to the first dose of study drug and must meet all inclusion and none of the exclusion criteria. The patients must be thoroughly informed about all aspects of the study, all evaluations as required per protocol and all regulatory requirements for informed consent.

Period 1

Period 1 title	Phase I
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

n.a.

Arms

Arm title	Phase I

Arm description:

Contains only patients in Phase I

Arm type	Experimental
Investigational medicinal product name	Erbitux
Investigational medicinal product code	L01XC06
Other name	Cetuximab
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Total 1900 mg/m2 milligram(s)/square meter

Number of subjects in period 1[1]	Phase I
Started	12
Completed	12

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Due to limitations of the database, only baseline values for Phase I are reported.

Period 2

Period 2 title	Phase II
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Phase II

Arm description:

Nine patients left the study at the end of Phase I. Three patients transfered from Phase I to Phase II and 23 patients were newly recruited in Phase II.

Arm type	Experimental
Investigational medicinal product name	Erbitux
Investigational medicinal product code	L01XC06
Other name	Cetuximab
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Total 1900 mg/m2 milligram(s)/square meter

Investigational medicinal product name	Oxaliplatin
Investigational medicinal product code	ATC L01XA03 - Oxaliplatin
Other name	Eloxatin
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Total: 200 mg/m2 milligram(s)/square meter

Number of subjects in period 2	Phase II
Started	12
Completed	18
Not completed	17
Adverse event, serious fatal	6
Consent withdrawn by subject	1
AE non fatal in Phase I	1
Adverse event, non-fatal	1
Lost to follow-up in Phase I	1
Regular end of Phase I	7
Joined	23
Regular start of Phase II	23

Baseline characteristics

Reporting groups	
Reporting group title	Phase I

Reporting group description: -

Reporting group values	Phase I	Total	
Number of subjects	12	12	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	60.9		
full range (min-max)	48 to 71	-	
Gender categorical Units: Subjects			
Female	2	2	
Male	10	10	

End points

End points reporting groups

Reporting group title	Phase I
Reporting group description:	
Contains only patients in Phase I	
Reporting group title	Phase II
Reporting group description:	
Nine patients left the study at the end of Phase I. Three patients transfered from Phase I to Phase II and 23 patients were newly recruited in Phase II.	

Primary: Dose finding Phase I

End point title	Dose finding Phase I[1]
End point description:	
No dose limiting toxicities were observed throughout phase I of the study, therefore phase II continued with dose level 3.	
End point type	Primary
End point timeframe:	
Phase I of the study	

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: This endpoint is descriptive.

End point values	Phase I			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: patients				
Dose-limiting toxicities	0			
No dose-limiting toxicities	12			

Statistical analyses

No statistical analyses for this end point

Primary: Response rate Phase II

End point title	Response rate Phase II
End point description:	
Number of patients with histological remission (Becker) was 55.6%, i.e. greater than 50%, therefore the primary endpoint was reached. The two-sided 95% Clopper-Pearson exact KI for the poin estimate was (22.0%, 69.0%).	
End point type	Primary
End point timeframe:	
Phase II of the study	

End point values	Phase II	Phase I		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	3[2]		
Units: patients				
Response	10	0		
No response	6	0		

Notes:

[2] - No patietns from Phase I were included in this analysis

Statistical analyses

Statistical analysis title	Exact CI

Statistical analysis description:

Clopper-Pearson exact 95% confidence interval for the response rate. The analysis is based on the 18 evaluable patients from Phase II. Due to database limitations, some (3) patients from Phase I needed to be included in the total. Please note that the analysis did not include the 3 patients from Phase I.

Comparison groups	Phase I v Phase II
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other[3]
Parameter estimate	Response rate
Point estimate	0.556
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.22
upper limit	0.69

Notes:

[3] - Confidence interval

Secondary: Resection rate

End point title	Resection rate

End point description:

End point type	Secondary

End point timeframe:

after surgery

End point values	Phase II			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: patients				
R0	20			
R1	4			

R2	1			
missing	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:

The 1-year OS rate was 71.9%. The 2-year OS rate was 53.1%. The 5-year OS rate was 30.1%.

End point type	Secondary

End point timeframe:

Entire study

End point values	Phase II			
Subject group type	Reporting group			
Number of subjects analysed	35[4]			
Units: days				
arithmetic mean (standard error)	969 (± 117)			

Notes:

[4] - Contains all patients from Phase I and Phase II

Statistical analyses

No statistical analyses for this end point

Secondary: Event-free survival

End point title	Event-free survival

End point description:

Time to relapse, progress, or death.

End point type	Secondary

End point timeframe:

entire study

End point values	Phase II			
Subject group type	Reporting group			
Number of subjects analysed	35[5]			
Units: days				
arithmetic mean (standard error)	578 (± 67)			

Notes:
[5] - Contains all patients from Phase I and Phase II

Statistical analyses

No statistical analyses for this end point

Secondary: Metabolic response rate (mono-chemo)

End point title	Metabolic response rate (mono-chemo)

End point description:

End point type	Secondary

End point timeframe:
Phase II of the study after 2 weeks of Cetuximab Mono Chemotherapy.

End point values	Phase II			
Subject group type	Reporting group			
Number of subjects analysed	21[6]			
Units: patients				
PET-responder	8			
PET- non-responder	13			

Notes:
[6] - Only 21 patients underwent this investigation.

Statistical analyses

No statistical analyses for this end point

Secondary: Metabolic response rate (radio-chemo)

End point title	Metabolic response rate (radio-chemo)

End point description:

End point type	Secondary

End point timeframe:
During phase II of the study, after 2 weeks of radio-chemo therapy.

End point values	Phase II			
Subject group type	Reporting group			
Number of subjects analysed	19[7]			
Units: patients				
PET-responder	10			
PET-non-responder	9			

Notes:

[7] - Only 19 patients underwent this investigation.

Statistical analyses

No statistical analyses for this end point

Secondary: Post-OP complications

End point title	Post-OP complications

End point description:

End point type	Secondary

End point timeframe:

up to 30 days post surgery

End point values	Phase II			
Subject group type	Reporting group			
Number of subjects analysed	27[8]			
Units: complications				
death	2			

Notes:

[8] - 27 patients had surgery during the study

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Entire study, phase I and II together.	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	13.1
Reporting groups	
Reporting group title	Phase I and II
Reporting group description: Contains all patients who started the study at any point.	

Serious adverse events	Phase I and II		
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 35 (85.71%)		
number of deaths (all causes)	22		
number of deaths resulting from adverse events	18		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Oesophageal adenocarcinoma recurrent			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Malignant melanoma			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oesophageal carcinoma recurrent			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metastases to bone			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Tracheal cancer			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metastases to lung			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Oncologic complication			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neoplasm progression			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Haemorrhage			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pain			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Haemorrhage			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertonia			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Jugular vein thrombosis			

subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Circulatory collapse				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Necrosis ischaemic				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral arterial occlusive disease				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Axillary vein thrombosis				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Venous thrombosis limb				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
Tracheostomy tube removal				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stent removal				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oesophagectomy				

subjects affected / exposed	2 / 35 (5.71%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Oesophagostomy				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stent placement				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Pyrexia				
subjects affected / exposed	4 / 35 (11.43%)			
occurrences causally related to treatment / all	2 / 6			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	2 / 35 (5.71%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Mucosal inflammation				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Systemic inflammatory response syndrome				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Death				

subjects affected / exposed	18 / 35 (51.43%)			
occurrences causally related to treatment / all	2 / 18			
deaths causally related to treatment / all	2 / 18			
Impaired healing				
subjects affected / exposed	2 / 35 (5.71%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Hypersensitivity				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Mediastinal disorder				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute respiratory failure				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute respiratory distress syndrome				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	4 / 35 (11.43%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Chylothorax				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Haemoptysis			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Stridor			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tracheal stenosis			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Inflammation			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural			

complications				
Anastomotic stenosis				
subjects affected / exposed	3 / 35 (8.57%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Anastomotic complication				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Anastomotic leak				
subjects affected / exposed	6 / 35 (17.14%)			
occurrences causally related to treatment / all	2 / 7			
deaths causally related to treatment / all	0 / 0			
Fracture				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tracheostomy malfunction				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Procedural complication				
subjects affected / exposed	2 / 35 (5.71%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hernia				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Cardiac failure				
subjects affected / exposed	2 / 35 (5.71%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			

Cardio-respiratory arrest				
subjects affected / exposed	2 / 35 (5.71%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Tachyarrhythmia				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Tachycardia				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Orthostatic intolerance				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Paresis				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Dizziness postural				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Glaucoma				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Visual impairment				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	7 / 35 (20.00%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 0		
Oesophageal stenosis			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Fistula			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Erysipelas			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Febrile infection			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Iatrogenic infection			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infection			

subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mediastinitis				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural infection				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	2 / 35 (5.71%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Wound infection staphylococcal				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypovolaemia				

subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malnutrition			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Phase I and II		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 35 (100.00%)		
Injury, poisoning and procedural complications			
Radiation skin injury			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Postoperative delirium			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Vascular disorders			
Hypotonia			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Thrombosis			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	3		
Tachyarrhythmia			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Nervous system disorders			

Taste disorder subjects affected / exposed occurrences (all)	3 / 35 (8.57%) 7		
Paraesthesia subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 2		
Dizziness subjects affected / exposed occurrences (all)	5 / 35 (14.29%) 9		
General disorders and administration site conditions			
Asthenia subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 2		
Chest pain subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 2		
Inflammation subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 2		
Fatigue subjects affected / exposed occurrences (all)	4 / 35 (11.43%) 6		
Pyrexia subjects affected / exposed occurrences (all)	8 / 35 (22.86%) 11		
Mucosal inflammation subjects affected / exposed occurrences (all)	9 / 35 (25.71%) 21		
Pain subjects affected / exposed occurrences (all)	4 / 35 (11.43%) 4		
Systemic inflammatory response syndrome subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 2		
Gastrointestinal disorders			

Ascites			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	13 / 35 (37.14%)		
occurrences (all)	21		
Dysphagia			
subjects affected / exposed	24 / 35 (68.57%)		
occurrences (all)	64		
Vomiting			
subjects affected / exposed	13 / 35 (37.14%)		
occurrences (all)	21		
Constipation			
subjects affected / exposed	9 / 35 (25.71%)		
occurrences (all)	16		
Oesophagitis			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Odynophagia			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	3		
Stomatitis			
subjects affected / exposed	4 / 35 (11.43%)		
occurrences (all)	4		
Nausea			
subjects affected / exposed	17 / 35 (48.57%)		
occurrences (all)	30		
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	4 / 35 (11.43%)		
occurrences (all)	5		
Cough			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
Pleural effusion			

subjects affected / exposed	10 / 35 (28.57%)		
occurrences (all)	12		
Respiratory failure			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	5 / 35 (14.29%)		
occurrences (all)	17		
Rash			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
Dermatitis acneiform			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	7		
Erythema			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Pruritus			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	7		
Dry skin			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Infections and infestations			
Infection			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	3		
Mediastinitis			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Nasopharyngitis			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Oral candidiasis			

subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Pneumonia			
subjects affected / exposed	8 / 35 (22.86%)		
occurrences (all)	9		
sepsis			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Wound infection			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	3		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	8 / 35 (22.86%)		
occurrences (all)	19		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/19549707