Clinical trial results:
A phase II study evaluating the combination of cetuximab with radiotherapy and concurrent chemotherapy with cisplatin and pemetrexed in the treatment of stage III inoperable non-squamous non-small cell lung cancer (NSCLC)

Summary

EudraCT number	2009-012412-41
Trial protocol	FR
Global end of trial date	31 December 2015

Results information

Result version number	v1 (current)
This version publication date	19 December 2020
First version publication date	19 December 2020

Trial information

Trial identification

Sponsor protocol code	IFCT-0803

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01102231
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	IFCT
Sponsor organisation address	10 rue de la Grange-Batelière, PARIS, France, 75009
Public contact	Responsable communication, IFCT, 33 0156811046, contact@ifct.fr
Scientific contact	Responsable communication, IFCT, 33 0156811046, contact@ifct.fr

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	15 July 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 December 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Efficacy (Disease control rate after 16 weeks)

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 March 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 106
Worldwide total number of subjects	106
EEA total number of subjects	106

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)	88
From 65 to 84 years	18
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The patients included in this study were recruited in 25 sites located in France from March 2010 until January 2014.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	106
Number of subjects completed	106

Period 1

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

Arms

Arm title	Cetuximab + chemo radiotherapy

Arm description:

Patients received weekly cetuximab (loading dose 400mg/m2Day 1, Week 1; subsequent weekly 250mg/m2doses until two weeks post-radiotherapy). Chemotherapy comprised cisplatin (75mg/m2) and pemetrexed (500mg/m2), both delivered on Day 1 of a 21-day cycle of maximally four. Irradiation (maximally 66Gy) started on Day 22.

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

Dosage and administration details:

D1 at an induction dose of 400 mg/m², and then once a week during the concurrent chemotherapy i.e. on D8, D15, D22, D29, D36, D43, D50, D57,
D64, D71 and D78 at a maintenance dose of 250 mg/m².

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

Dosage and administration details:

Pemetrexed 500 mg/m² was administered on D1 of a 21-day cycle for a total of 4 cycles

Investigational medicinal product name	Cisplatine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatin 75 mg/m² was administered on D1 of a 21-day cycle for a total of 4 cycles

Number of subjects in period 1	Cetuximab + chemo radiotherapy
Started	106
Completed	91
Not completed	15
Adverse event, serious fatal	2
Patients did not received any treatment	4
Patient's choice	1
Adverse event, non-fatal	3
Not eligible patient	3
Lack of efficacy	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	106	106	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	88	88	
From 65-84 years	18	18	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	55.97		
standard deviation	± 8.96	-	
Gender categorical Units: Subjects			
Female	39	39	
Male	67	67	
Weight loss Units: Subjects			
<=5%	80	80	
> 5%	26	26	
Smoking status Units: Subjects			
No	6	6	
Yes	100	100	
Cancer Stage Units: Subjects			
Stage IIIA	53	53	
Stage IIIB	51	51	
Stage IV	2	2	
Histological subtype Units: Subjects			
Sarcomatoid	2	2	
Adenosquamous	1	1	
Adenocarcinoma without bronchoalveolar component	82	82	
Non Small Cell	14	14	
Neuroendocrine carcinoma	1	1	

Non squamous Non Small cell	6	6	
ECOG Perfomans Status Units: Subjects			
PS 0	63	63	
PS 1	43	43	
Unresectability cause Units: Subjects			
Anatomical	100	100	
Functional	6	6	
Weight Units: kilogram(s)			
arithmetic mean	71.6		
standard deviation	± 14.66	-	
Number of pack-years Units: Pack-years			
arithmetic mean	42.42		
standard deviation	± 22.34	-	

End points

End points reporting groups

Reporting group title	Cetuximab + chemo radiotherapy
Reporting group description:	
Patients received weekly cetuximab (loading dose 400mg/m2Day 1, Week 1; subsequent weekly 250mg/m2doses until two weeks post-radiotherapy). Chemotherapy comprised cisplatin (75mg/m2) and pemetrexed (500mg/m2), both delivered on Day 1 of a 21-day cycle of maximally four. Irradiation (maximally 66Gy) started on Day 22.	
Subject analysis set title	Eligible population
Subject analysis set type	Per protocol
Subject analysis set description:	
Patients without deviation at inclusion.	
Subject analysis set title	Safety population
Subject analysis set type	Safety analysis
Subject analysis set description:	
Patients who received at least one protocol treatment	

Primary: Percentage of patients with disease control rate

End point title	Percentage of patients with disease control rate[1]
End point description:	
End point type	Primary
End point timeframe:	
16 weeks after inclusion	

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: Single arm study

End point values	Cetuximab + chemo radiotherapy			
Subject group type	Reporting group			
Number of subjects analysed	99			
Units: percent				
number (confidence interval 95%)	89.9 (84 to 95.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (median)

End point title	Overall survival (median)
End point description:	
End point type	Secondary
End point timeframe:	
Overall survival is defined as time between date of inclusion and all-cause death	

End point values	Eligible population			
Subject group type	Subject analysis set			
Number of subjects analysed	99			
Units: months				
number (confidence interval 95%)	35.8 (23.5 to 35.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: 6-month survival rate

End point title	6-month survival rate

End point description:

End point type	Secondary

End point timeframe:

6 months after inclusion

End point values	Eligible population			
Subject group type	Subject analysis set			
Number of subjects analysed	99			
Units: percent				
number (confidence interval 95%)	96.0 (89.6 to 98.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: 9-month survival rate

End point title	9-month survival rate

End point description:

End point type	Secondary

End point timeframe:

9 months after inclusion

End point values	Eligible population			
Subject group type	Subject analysis set			
Number of subjects analysed	99			
Units: percent				
number (confidence interval 95%)	86.9 (78.5 to 92.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: 12-month survival rate

End point title	12-month survival rate

End point description:

End point type	Secondary

End point timeframe:

12 months after inclusion

End point values	Eligible population			
Subject group type	Subject analysis set			
Number of subjects analysed	99			
Units: percent				
number (confidence interval 95%)	74.7 (65.0 to 82.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: 18-month survival rate

End point title	18-month survival rate

End point description:

End point type	Secondary

End point timeframe:

18 months after inclusion

End point values	Eligible population			
Subject group type	Subject analysis set			
Number of subjects analysed	99			
Units: percent				
number (confidence interval 95%)	68.7 (58.6 to 76.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free survival (median)

End point title	Progression Free survival (median)

End point description:

End point type	Secondary

End point timeframe:

Progression-free survival is defined as time between date of inclusion and progression or all-cause death.

End point values	Eligible population			
Subject group type	Subject analysis set			
Number of subjects analysed	99			
Units: Months				
number (confidence interval 95%)	14.4 (11.2 to 18.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: 6-month progression-free survival rate

End point title	6-month progression-free survival rate

End point description:

End point type	Secondary

End point timeframe:

6 months after inclusion

End point values	Eligible population			
Subject group type	Subject analysis set			
Number of subjects analysed	99			
Units: percent				
number (confidence interval 95%)	78.8 (69.3 to 85.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: 9-month progression-free survival rate

End point title	9-month progression-free survival rate

End point description:

End point type	Secondary

End point timeframe:

9 months after inclusion

End point values	Eligible population			
Subject group type	Subject analysis set			
Number of subjects analysed	99			
Units: percent				
number (confidence interval 95%)	64.6 (54.4 to 73.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: 12-month progression-free survival rate

End point title	12-month progression-free survival rate

End point description:

End point type	Secondary

End point timeframe:

12 months after inclusion

End point values	Eligible population			
Subject group type	Subject analysis set			
Number of subjects analysed	99			
Units: percent				
number (confidence interval 95%)	57.6 (47.2 to 66.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: 18-month progression-free survival rate

End point title	18-month progression-free survival rate

End point description:

End point type	Secondary

End point timeframe:

18 months after inclusion

End point values	Eligible population			
Subject group type	Subject analysis set			
Number of subjects analysed	99			
Units: percent				
number (confidence interval 95%)	42.4 (32.6 to 51.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate at 16 weeks

End point title	Overall Response Rate at 16 weeks

End point description:

End point type	Secondary

End point timeframe:

16 weeks after inclusion

End point values	Eligible population			
Subject group type	Subject analysis set			
Number of subjects analysed	99			
Units: percent				
number (confidence interval 95%)	62.6 (0 to 70.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Stable disease rate at 16 weeks

End point title	Stable disease rate at 16 weeks

End point description:

End point type	Secondary

End point timeframe:

16 weeks after inclusion

End point values	Eligible population			
Subject group type	Subject analysis set			
Number of subjects analysed	99			
Units: percent				
number (confidence interval 95%)	27.3 (18.5 to 36.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progressive disease rate at 16 weeks

End point title	Progressive disease rate at 16 weeks

End point description:

End point type	Secondary

End point timeframe:

16 weeks after inclusion

End point values	Eligible population			
Subject group type	Subject analysis set			
Number of subjects analysed	99			
Units: percent				
number (confidence interval 95%)	3.0 (0.0 to 6.4)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The adverse events have to be reported from inclusion to 30 day following the end of administration of study treatments.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21

Reporting groups

Reporting group title	Safety Population

Reporting group description:

The safety population will be defined as all patients who received at least one dose of treatment.

Serious adverse events	Safety Population		
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 102 (25.49%)		
number of deaths (all causes)	51		
number of deaths resulting from adverse events			
Vascular disorders			
Phlebitis superficial			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	4 / 102 (3.92%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 102 (1.96%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Fatigue			

subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			
subjects affected / exposed	7 / 102 (6.86%)		
occurrences causally related to treatment / all	5 / 7		
deaths causally related to treatment / all	0 / 0		
Death			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Hyperthermia			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malaise			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Lung disorder				
subjects affected / exposed	3 / 102 (2.94%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	1 / 1			
Respiratory failure				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Asthma				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Haemoglobin decreased				
subjects affected / exposed	2 / 102 (1.96%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Neutrophil count decreased				
subjects affected / exposed	2 / 102 (1.96%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Platelet count decreased				
subjects affected / exposed	2 / 102 (1.96%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Expired product administered				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Subdural haematoma			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pericardial effusion			
subjects affected / exposed	2 / 102 (1.96%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Tachycardia			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Carotid artery aneurysm			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Bone marrow failure			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Febrile bone marrow aplasia			

subjects affected / exposed	2 / 102 (1.96%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	5 / 102 (4.90%)			
occurrences causally related to treatment / all	5 / 5			
deaths causally related to treatment / all	0 / 0			
Anaemia				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Eye pain				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Colitis				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	3 / 102 (2.94%)			
occurrences causally related to treatment / all	4 / 4			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Faecaloma				

subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	3 / 102 (2.94%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Oesophagitis				
subjects affected / exposed	4 / 102 (3.92%)			
occurrences causally related to treatment / all	4 / 4			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	4 / 102 (3.92%)			
occurrences causally related to treatment / all	5 / 5			
deaths causally related to treatment / all	0 / 0			
Aphasia				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis				
subjects affected / exposed	2 / 102 (1.96%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Palmar-plantar erythrodysaesthesia syndrome				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Acute kidney injury				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Haematuria			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	2 / 102 (1.96%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Device related infection			
subjects affected / exposed	3 / 102 (2.94%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	2 / 102 (1.96%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infective exacerbation of chronic obstructive airways disease			

subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 102 (1.96%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypocalcaemia			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	3 / 102 (2.94%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0.5 %

Non-serious adverse events	Safety Population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	100 / 102 (98.04%)		
Vascular disorders			
Acrosyndrom			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Hematoma			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	2		
Orthostatic hypotension			

subjects affected / exposed	2 / 102 (1.96%)		
occurrences (all)	4		
Thrombosis			
subjects affected / exposed	3 / 102 (2.94%)		
occurrences (all)	7		
General disorders and administration site conditions			
Alopecia			
subjects affected / exposed	14 / 102 (13.73%)		
occurrences (all)	28		
Asthenia			
subjects affected / exposed	78 / 102 (76.47%)		
occurrences (all)	250		
Chest pain			
subjects affected / exposed	19 / 102 (18.63%)		
occurrences (all)	47		
Dehydration			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Edema limb			
subjects affected / exposed	7 / 102 (6.86%)		
occurrences (all)	10		
Fatigue			
subjects affected / exposed	5 / 102 (4.90%)		
occurrences (all)	17		
Fever			
subjects affected / exposed	14 / 102 (13.73%)		
occurrences (all)	23		
Hypothermia			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Inflammation			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Localized edema			

subjects affected / exposed occurrences (all) Malaise subjects affected / exposed occurrences (all) Night sweats subjects affected / exposed occurrences (all) oedema face subjects affected / exposed occurrences (all) Pain subjects affected / exposed occurrences (all) Reduced general condition subjects affected / exposed occurrences (all) Vertigo subjects affected / exposed occurrences (all) Weight loss subjects affected / exposed occurrences (all)	2 / 102 (1.96%) 6 2 / 102 (1.96%) 2 2 / 102 (1.96%) 3 1 / 102 (0.98%) 1 5 / 102 (4.90%) 17 5 / 102 (4.90%) 7 6 / 102 (5.88%) 10 19 / 102 (18.63%) 50		
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	2 / 102 (1.96%) 4		
Reproductive system and breast disorders Balanitis subjects affected / exposed occurrences (all)	1 / 102 (0.98%) 1		
Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all) Bronchitis	1 / 102 (0.98%) 2		

subjects affected / exposed	4 / 102 (3.92%)			
occurrences (all)	8			
Chronic obstructive pulmonary disease				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences (all)	1			
Cough				
subjects affected / exposed	38 / 102 (37.25%)			
occurrences (all)	94			
Dysphonia				
subjects affected / exposed	10 / 102 (9.80%)			
occurrences (all)	28			
Dyspnoea				
subjects affected / exposed	39 / 102 (38.24%)			
occurrences (all)	94			
Epistaxis				
subjects affected / exposed	13 / 102 (12.75%)			
occurrences (all)	16			
Expectoration				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences (all)	4			
Haemoptysis				
subjects affected / exposed	6 / 102 (5.88%)			
occurrences (all)	9			
Hypoxia				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences (all)	1			
Pharyngitis				
subjects affected / exposed	4 / 102 (3.92%)			
occurrences (all)	4			
Pneumopathy				
subjects affected / exposed	4 / 102 (3.92%)			
occurrences (all)	4			
Pulmonary embolism				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences (all)	3			

Respiratory disorder			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed	4 / 102 (3.92%)		
occurrences (all)	7		
Rhinorrhoea			
subjects affected / exposed	3 / 102 (2.94%)		
occurrences (all)	3		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	5 / 102 (4.90%)		
occurrences (all)	9		
Confusion			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	2 / 102 (1.96%)		
occurrences (all)	4		
Impatience			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Sleep disorder			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	4		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 102 (3.92%)		
occurrences (all)	13		
Alkaline phosphatase increased			
subjects affected / exposed	4 / 102 (3.92%)		
occurrences (all)	13		
Aspartate aminotransferase increased			

subjects affected / exposed	2 / 102 (1.96%)		
occurrences (all)	6		
Creatinine increased			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	4		
Gamma-glutamyltransferase increased			
subjects affected / exposed	4 / 102 (3.92%)		
occurrences (all)	14		
Haemoglobin decreased			
subjects affected / exposed	63 / 102 (61.76%)		
occurrences (all)	217		
Hyperkalemia			
subjects affected / exposed	2 / 102 (1.96%)		
occurrences (all)	5		
LDH increased			
subjects affected / exposed	4 / 102 (3.92%)		
occurrences (all)	14		
Injury, poisoning and procedural complications			
Expired product administered			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Congenital, familial and genetic disorders			
Ichthyosis			
subjects affected / exposed	2 / 102 (1.96%)		
occurrences (all)	3		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Cardiac failure			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	5 / 102 (4.90%)		
occurrences (all)	7		

Hypotension subjects affected / exposed occurrences (all)	3 / 102 (2.94%) 4		
Tachycardia subjects affected / exposed occurrences (all)	4 / 102 (3.92%) 5		
Nervous system disorders Clubbing subjects affected / exposed occurrences (all)	1 / 102 (0.98%) 1		
Dysaesthesia subjects affected / exposed occurrences (all)	1 / 102 (0.98%) 5		
Headache subjects affected / exposed occurrences (all)	3 / 102 (2.94%) 3		
Laryngoparalysis subjects affected / exposed occurrences (all)	1 / 102 (0.98%) 1		
Memory impairment subjects affected / exposed occurrences (all)	1 / 102 (0.98%) 2		
Neurological disorder subjects affected / exposed occurrences (all)	1 / 102 (0.98%) 1		
Neuropathy subjects affected / exposed occurrences (all)	7 / 102 (6.86%) 8		
Nystagmus subjects affected / exposed occurrences (all)	1 / 102 (0.98%) 1		
Paresthesia subjects affected / exposed occurrences (all)	7 / 102 (6.86%) 12		
Peripheral sensory neuropathy			

subjects affected / exposed	2 / 102 (1.96%)		
occurrences (all)	4		
Sensory neuropathy hereditary			
subjects affected / exposed	3 / 102 (2.94%)		
occurrences (all)	4		
Smell alteration			
subjects affected / exposed	2 / 102 (1.96%)		
occurrences (all)	5		
Tremor			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Hyperleukocytosis			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Leukopenia			
subjects affected / exposed	3 / 102 (2.94%)		
occurrences (all)	12		
Lymphopenia			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	3		
Neutrophil count decreased			
subjects affected / exposed	80 / 102 (78.43%)		
occurrences (all)	234		
Platelet count decreased			
subjects affected / exposed	62 / 102 (60.78%)		
occurrences (all)	178		
Platelet count increased			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Ear disorder			

subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Hearing loss			
subjects affected / exposed	3 / 102 (2.94%)		
occurrences (all)	11		
Otitis			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	4		
Tinnitus			
subjects affected / exposed	10 / 102 (9.80%)		
occurrences (all)	28		
Eye disorders			
Conjunctivitis			
subjects affected / exposed	9 / 102 (8.82%)		
occurrences (all)	13		
dry eye syndrome			
subjects affected / exposed	4 / 102 (3.92%)		
occurrences (all)	7		
Eye disorder			
subjects affected / exposed	3 / 102 (2.94%)		
occurrences (all)	4		
Eye irritation			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Eye pain			
subjects affected / exposed	2 / 102 (1.96%)		
occurrences (all)	3		
watering eyes			
subjects affected / exposed	4 / 102 (3.92%)		
occurrences (all)	6		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 102 (3.92%)		
occurrences (all)	7		
Anal pain			

subjects affected / exposed	1 / 102 (0.98%)			
occurrences (all)	1			
Anorexia				
subjects affected / exposed	45 / 102 (44.12%)			
occurrences (all)	106			
Aphagia				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences (all)	2			
Constipation				
subjects affected / exposed	39 / 102 (38.24%)			
occurrences (all)	83			
Diarrhoea				
subjects affected / exposed	23 / 102 (22.55%)			
occurrences (all)	34			
Dysgeusia				
subjects affected / exposed	6 / 102 (5.88%)			
occurrences (all)	8			
Dyspepsia				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences (all)	1			
Dysphagia				
subjects affected / exposed	50 / 102 (49.02%)			
occurrences (all)	120			
Oesophagitis				
subjects affected / exposed	65 / 102 (63.73%)			
occurrences (all)	181			
Flatulence				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences (all)	1			
Gastralgia				
subjects affected / exposed	18 / 102 (17.65%)			
occurrences (all)	24			
Gastroenteritis				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences (all)	1			
Gastrooesophageal reflux				

subjects affected / exposed	8 / 102 (7.84%)		
occurrences (all)	12		
Gingival pain			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Gingivitis			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Haemorrhoids			
subjects affected / exposed	5 / 102 (4.90%)		
occurrences (all)	9		
Nausea			
subjects affected / exposed	76 / 102 (74.51%)		
occurrences (all)	217		
Odynophagia			
subjects affected / exposed	4 / 102 (3.92%)		
occurrences (all)	8		
Oral mucosal irritation			
subjects affected / exposed	44 / 102 (43.14%)		
occurrences (all)	92		
Pyrosis			
subjects affected / exposed	6 / 102 (5.88%)		
occurrences (all)	10		
Stomatitis			
subjects affected / exposed	2 / 102 (1.96%)		
occurrences (all)	2		
Tooth disorder			
subjects affected / exposed	3 / 102 (2.94%)		
occurrences (all)	7		
Vomiting			
subjects affected / exposed	37 / 102 (36.27%)		
occurrences (all)	69		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	23 / 102 (22.55%)		
occurrences (all)	80		

Body hair increased				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences (all)	2			
Burning skin				
subjects affected / exposed	3 / 102 (2.94%)			
occurrences (all)	6			
Chalazion				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences (all)	1			
Dermatitis				
subjects affected / exposed	27 / 102 (26.47%)			
occurrences (all)	58			
Desquamation				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences (all)	2			
Dry skin				
subjects affected / exposed	30 / 102 (29.41%)			
occurrences (all)	92			
Erysipelas				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences (all)	1			
Erythema				
subjects affected / exposed	21 / 102 (20.59%)			
occurrences (all)	46			
Folliculitis				
subjects affected / exposed	36 / 102 (35.29%)			
occurrences (all)	124			
Furuncle				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences (all)	2			
Hand and foot syndrome				
subjects affected / exposed	2 / 102 (1.96%)			
occurrences (all)	2			
Nail disorder				
subjects affected / exposed	5 / 102 (4.90%)			
occurrences (all)	15			

Paronychia			
subjects affected / exposed	7 / 102 (6.86%)		
occurrences (all)	10		
Pruritus			
subjects affected / exposed	7 / 102 (6.86%)		
occurrences (all)	10		
Purpura			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	32 / 102 (31.37%)		
occurrences (all)	114		
Skin disorder			
subjects affected / exposed	12 / 102 (11.76%)		
occurrences (all)	26		
Skin eruption			
subjects affected / exposed	16 / 102 (15.69%)		
occurrences (all)	46		
Skin fissures			
subjects affected / exposed	5 / 102 (4.90%)		
occurrences (all)	10		
Skin hyperpigmentation			
subjects affected / exposed	2 / 102 (1.96%)		
occurrences (all)	2		
Skin ulceration			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Renal and urinary disorders			
Hiccough			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Nocturnal polyuria			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Prostatic disorder			

subjects affected / exposed	2 / 102 (1.96%)		
occurrences (all)	2		
Proteinuria			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Renal colic			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Renal disorder			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	3		
Renal failure			
subjects affected / exposed	8 / 102 (7.84%)		
occurrences (all)	21		
Urinary tract pain			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	5 / 102 (4.90%)		
occurrences (all)	15		
Bone pain			
subjects affected / exposed	3 / 102 (2.94%)		
occurrences (all)	5		
Cramps			
subjects affected / exposed	2 / 102 (1.96%)		
occurrences (all)	3		
Flank pain			
subjects affected / exposed	2 / 102 (1.96%)		
occurrences (all)	2		
Joint pain			
subjects affected / exposed	3 / 102 (2.94%)		
occurrences (all)	3		
Myalgia			

subjects affected / exposed	3 / 102 (2.94%)		
occurrences (all)	4		
Pain in extremity			
subjects affected / exposed	4 / 102 (3.92%)		
occurrences (all)	8		
Pain neck/shoulder			
subjects affected / exposed	3 / 102 (2.94%)		
occurrences (all)	5		
Rib pain			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	2		
Infections and infestations			
Cystitis			
subjects affected / exposed	3 / 102 (2.94%)		
occurrences (all)	4		
herpes labialis			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	2		
Herpes NOS			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Infection			
subjects affected / exposed	3 / 102 (2.94%)		
occurrences (all)	7		
Localized infection			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	2		
Lymphangitis			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Mycosis			
subjects affected / exposed	6 / 102 (5.88%)		
occurrences (all)	7		
Oral candida			
subjects affected / exposed	3 / 102 (2.94%)		
occurrences (all)	3		

Tooth infection subjects affected / exposed occurrences (all)	1 / 102 (0.98%) 1		
Urethral infection subjects affected / exposed occurrences (all)	1 / 102 (0.98%) 2		
Urinary tract infection subjects affected / exposed occurrences (all)	4 / 102 (3.92%) 6		
Vaginal infection subjects affected / exposed occurrences (all)	1 / 102 (0.98%) 3		
Vulvitis subjects affected / exposed occurrences (all)	1 / 102 (0.98%) 1		
Metabolism and nutrition disorders Hypocalcemia subjects affected / exposed occurrences (all)	1 / 102 (0.98%) 1		
Hypokalaemia subjects affected / exposed occurrences (all)	7 / 102 (6.86%) 14		
Hypomagnesaemia subjects affected / exposed occurrences (all)	5 / 102 (4.90%) 18		
Hyponatraemia subjects affected / exposed occurrences (all)	2 / 102 (1.96%) 8		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 September 2011	Clarification on exclusion criteria and toxicity management for cetuximab.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The study was not randomized.

Notes: