Clinical trial results:
Effektivitätsoptimierte und toxizitätsreduzierte Therapie des metastasierten Kolorektalkarzinoms in der First-line Therapie

Summary

EudraCT number	2006-002744-28
Trial protocol	DE
Global end of trial date	16 April 2014

Results information

Result version number	v1 (current)
This version publication date	25 June 2016
First version publication date	25 June 2016
Summary attachment (see zip file)	ERBIMOX Synopsis (20150415_ERBIMOX_Synopsis_CSR_V2.0.pdf)

Trial information

Trial identification

Sponsor protocol code	IOM-510-2

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	iOMEDICO AG
Sponsor organisation address	Hanferstraße 28, Freiburg, Germany, 79108
Public contact	iOMEDICO AG Dr. Sabine Busies Director BU Clinical Research, iOMEDICO AG Dr. Sabine Busies Director BU Clinical Research, 0049 0761 1524214, sabine.busies@iomedico.com
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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	No

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	15 April 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 April 2014
Global end of trial reached?	Yes
Global end of trial date	16 April 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To verify the superiority of a combined chemo-immuno-therapy compared to exclusive chemotherapy (ie, to demonstrate superiority of additional cetucimab to modified FOLFOX 7 compared to modified FOLFOX 7 alone) in first-line treatment of patients with KRAS wild-type metastatic colorectal cancer, in terms of objective response rate (ORR).

Protection of trial subjects:

The study was conducted in compliance with the protocol, according to ICH-GCP current local laws and regulations, and with the ethical principles laid down in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 October 2006
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	Germany: 191
Worldwide total number of subjects	191
EEA total number of subjects	191

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)	80
From 65 to 84 years	111
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The ERBIMOX study was an open-label, randomized, two-arm, multicenter, phase II study of first-line treatment in mCRC. Patients were randomly assigned (1:1) to receive modified FOLFOX7 with or without cetuximab. Patients were enrolled at office-based medical oncology practices.

Pre-assignment

Screening details:

Time of screening period: 30 days without a pre-assignment period. Patients were enrolled if inclusion and exclusion criteria were met. In total N = 196 patients were screened and randomized.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A - Optimox

Arm description:

Modified FOLFOX 7 was administred for 8 two-weekly cycles of induction period, stopping oxaliplatin during subsequent maintenance period persisting until disease progression.

Arm type	Active comparator
Investigational medicinal product name	modified FOLFOX 7
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Leucovorin (folinic acid, FA) 400 mg/m2
Fluorouracil (5-FU) 2,400 mg/m2 over 48 hours
Oxaliplatin 85 mg/m2 only for 8 two-weekly cycles (induction period)

Arm title	Arm B - Erbimox

Arm description:

Adding continously cetuximab to modified FOLFOX 7 for the 8 two-weekly induction period followed by subsequent maintanance period without oxaliplatin until disease progression.

Arm type	Experimental
Investigational medicinal product name	Cetuximab
Investigational medicinal product code	EMD271786
Other name	Erbitux
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Weekly 250 mg/m2 day 1 and day 8 of each two-weekly cycle; first cetuximab administration 400 mg/m2

Number of subjects in period 1	Arm A - Optimox	Arm B - Erbimox
Started	95	96
Completed	63	75
Not completed	32	21
KRAS mutation status unknown	15	12
KRAS mutation status positive	17	-
'KRAS tumor status positve '	-	9

Baseline characteristics

Reporting groups

Reporting group title	Arm A - Optimox

Reporting group description:

Modified FOLFOX 7 was administred for 8 two-weekly cycles of induction period, stopping oxaliplatin during subsequent maintenance period persisting until disease progression.

Reporting group title	Arm B - Erbimox

Reporting group description:

Adding continously cetuximab to modified FOLFOX 7 for the 8 two-weekly induction period followed by subsequent maintanance period without oxaliplatin until disease progression.

Reporting group values	Arm A - Optimox	Arm B - Erbimox	Total
Number of subjects	95	96	191
Age categorical			
Number of patients per category			
Units: Subjects			
18 - 64 years	45	35	80
>=65 years	50	61	111
Age continuous			
Units: years			
median	65.6	67.4	
full range (min-max)	38.4 to 77.8	38.9 to 82.6	-
Gender categorical			
Units: Subjects			
Female	27	34	61
Male	68	62	130
Site of tumor			
Units: Subjects			
Colon	48	52	100
Rectum	47	44	91

Subject analysis sets

Subject analysis set title	Modified Intent-to-treat
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All randomized patients with verified KRAS wild-type tumor, who received at least one dose of study medication.

Subject analysis set title	Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

Safety analysis set

Reporting group values	Modified Intent-to-treat	Safety	
Number of subjects	138	191	
Age categorical			
Number of patients per category			
Units: Subjects			

18 - 64 years	59	80	
>=65 years	79	111	

Age continuous Units: years			
median	66.9	67.2	
full range (min-max)	38.4 to 82.1	38.4 to 82.6	
Gender categorical Units: Subjects			
Female	43	61	
Male	95	130	
Site of tumor Units: Subjects			
Colon	67	100	
Rectum	71	91	

End points

End points reporting groups

Reporting group title	Arm A - Optimox
Reporting group description:	
Modified FOLFOX 7 was administred for 8 two-weekly cycles of induction period, stopping oxaliplatin during subsequent maintenance period persisting until disease progression.	
Reporting group title	Arm B - Erbimox
Reporting group description:	
Adding continously cetuximab to modified FOLFOX 7 for the 8 two-weekly induction period followed by subsequent maintanance period without oxaliplatin until disease progression.	
Subject analysis set title	Modified Intent-to-treat
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
All randomized patients with verified KRAS wild-type tumor, who received at least one dose of study medication.	
Subject analysis set title	Safety
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety analysis set	

Primary: Objective response rate

End point title	Objective response rate
End point description:	
End point type	Primary
End point timeframe:	
During treatment until disesase progression, death, or any cause of permanent treatment discontinuation	

End point values	Arm A - Optimox	Arm B - Erbimox	Modified Intent-to-treat	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	63[1]	75[2]	138	
Units: Number of complete and partial responses	34	48	82	

Notes:

[1] - Total of m-ITT analysis set

[2] - Total number of m-ITT analysis set

Statistical analyses

Statistical analysis title	Cochran-Mantel-Haenszel
Statistical analysis description:	
Comparison of response rates between treatment groups	
Comparison groups	Arm B - Erbimox v Arm A - Optimox

Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Cochran-Mantel-Haenszel
Parameter estimate	chi-square
Confidence interval	
level	95 %
sides	2-sided

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AE reporting whilst patients are on treatment, including 30 days follow-up period after permanent treatment discontinuation.

Adverse event reporting additional description:

Only grade 3/4 serious and non-serious adverse events are reported

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.3

Reporting groups

Reporting group title	Arm B - Erbimox

Reporting group description:

Cetuximab continuously administered to modified FOLFOX 7 during the induction period (ie, eight two-weekly cycles) and during the subsequent maintenance period without oxaliplatin until progressive disease, unacceptable toxicity or withdrawal of consent.

Reporting group title	Arm A Optimox

Reporting group description: -

Serious adverse events	Arm B - Erbimox	Arm A Optimox	
Total subjects affected by serious adverse events			
subjects affected / exposed	35 / 96 (36.46%)	25 / 95 (26.32%)	
number of deaths (all causes)	53	44	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	0 / 96 (0.00%)	2 / 95 (2.11%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian vein thrombosis			
subjects affected / exposed	0 / 96 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			

subjects affected / exposed	0 / 96 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Subileus			
subjects affected / exposed	1 / 96 (1.04%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device occlusion			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extravasation			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	2 / 96 (2.08%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 1	
Mucosal inflammation			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device dislocation			

subjects affected / exposed	0 / 96 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dispnoea			
subjects affected / exposed	1 / 96 (1.04%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	2 / 96 (2.08%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Biopsy liver			
subjects affected / exposed	0 / 96 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stoma site haemorrhage			
subjects affected / exposed	0 / 96 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			

subjects affected / exposed	0 / 96 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 96 (1.04%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 1	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 96 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 96 (1.04%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	2 / 96 (2.08%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	1 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			
subjects affected / exposed	0 / 96 (0.00%)	2 / 95 (2.11%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorder			

subjects affected / exposed	0 / 96 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 96 (0.00%)	2 / 95 (2.11%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coagulopathy			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemias NEC			
subjects affected / exposed	0 / 96 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 96 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 96 (4.17%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	4 / 35	0 / 25	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ileus			

subjects affected / exposed	0 / 96 (0.00%)	2 / 95 (2.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis haemorrhagic			
subjects affected / exposed	0 / 96 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 96 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	2 / 96 (2.08%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal pain			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	1 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Obstructive uropathy			
subjects affected / exposed	0 / 96 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus urethral			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	4 / 96 (4.17%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	4 / 35	1 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 96 (1.04%)	2 / 95 (2.11%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	0 / 96 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	2 / 96 (2.08%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			

Cachexia			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	2 / 96 (2.08%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Arm B - Erbimox	Arm A Optimox	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 96 (54.17%)	30 / 95 (31.58%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm progression			
subjects affected / exposed	0 / 96 (0.00%)	1 / 95 (1.05%)	
occurrences (all)	43	23	
Ovarian cancer			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences (all)	43	23	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences (all)	43	23	
Surgical and medical procedures			

Jejunostomy refashioning			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences (all)	43	23	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 96 (1.04%)	23 / 95 (24.21%)	
occurrences (all)	43	30	
Fatigue			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences (all)	43	23	
Mucosal inflammation			
subjects affected / exposed	2 / 96 (2.08%)	0 / 95 (0.00%)	
occurrences (all)	43	23	
Pain			
subjects affected / exposed	1 / 96 (1.04%)	1 / 95 (1.05%)	
occurrences (all)	43	23	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 96 (0.00%)	1 / 95 (1.05%)	
occurrences (all)	43	23	
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 96 (1.04%)	1 / 95 (1.05%)	
occurrences (all)	43	23	
Investigations			
Blood magnesium decreased			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences (all)	43	23	
Blood glucose increased			
subjects affected / exposed	0 / 96 (0.00%)	1 / 95 (1.05%)	
occurrences (all)	43	23	
Liver function test abnormal			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences (all)	43	23	
Nervous system disorders			

Convulsion			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences (all)	43	23	
Epilepsy			
subjects affected / exposed	0 / 96 (0.00%)	1 / 95 (1.05%)	
occurrences (all)	43	23	
Loss of consciousness			
subjects affected / exposed	0 / 96 (0.00%)	1 / 95 (1.05%)	
occurrences (all)	43	23	
Paraesthesia			
subjects affected / exposed	1 / 96 (1.04%)	1 / 95 (1.05%)	
occurrences (all)	43	23	
Polyneuropathy			
subjects affected / exposed	0 / 96 (0.00%)	1 / 95 (1.05%)	
occurrences (all)	43	23	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 96 (2.08%)	1 / 95 (1.05%)	
occurrences (all)	43	23	
Leukopenia			
subjects affected / exposed	0 / 96 (0.00%)	1 / 95 (1.05%)	
occurrences (all)	43	23	
Neutropenia			
subjects affected / exposed	0 / 96 (0.00%)	2 / 95 (2.11%)	
occurrences (all)	43	23	
Thrombocytopenia			
subjects affected / exposed	0 / 96 (0.00%)	1 / 95 (1.05%)	
occurrences (all)	43	23	
Gastrointestinal disorders			
Anal inflammation			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences (all)	43	23	
Constipation			
subjects affected / exposed	0 / 96 (0.00%)	3 / 95 (3.16%)	
occurrences (all)	43	23	
Diarrhoea			

subjects affected / exposed	3 / 96 (3.13%)	4 / 95 (4.21%)	
occurrences (all)	43	23	
Gastritis			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences (all)	43	23	
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences (all)	43	23	
Nausea			
subjects affected / exposed	2 / 96 (2.08%)	1 / 95 (1.05%)	
occurrences (all)	43	23	
Oesophagitis			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences (all)	43	23	
Vomiting			
subjects affected / exposed	0 / 96 (0.00%)	1 / 95 (1.05%)	
occurrences (all)	43	23	
Skin and subcutaneous tissue disorders			
Dermal and epidermal conditions NEC			
subjects affected / exposed	2 / 96 (2.08%)	0 / 95 (0.00%)	
occurrences (all)	43	23	
Dermatitis acneiform			
subjects affected / exposed	2 / 96 (2.08%)	0 / 95 (0.00%)	
occurrences (all)	43	23	
Nail bed inflammation			
subjects affected / exposed	2 / 96 (2.08%)	0 / 95 (0.00%)	
occurrences (all)	43	23	
Photosensitivity reaction			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences (all)	43	23	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	2 / 96 (2.08%)	2 / 95 (2.11%)	
occurrences (all)	43	23	
Musculoskeletal and connective tissue disorders			

Flank pain			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences (all)	43	23	
Fracture pain			
subjects affected / exposed	0 / 96 (0.00%)	1 / 95 (1.05%)	
occurrences (all)	43	23	
Limb discomfort			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences (all)	43	23	
Musculoskeletal stiffness			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences (all)	43	23	
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences (all)	43	23	
Device related infection			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences (all)	43	23	
Febrile infection			
subjects affected / exposed	0 / 96 (0.00%)	1 / 95 (1.05%)	
occurrences (all)	43	23	
Paronychia			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences (all)	43	23	
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences (all)	43	23	
Dehydration			
subjects affected / exposed	1 / 96 (1.04%)	0 / 95 (0.00%)	
occurrences (all)	43	23	
Hypokalaemia			
subjects affected / exposed	3 / 96 (3.13%)	0 / 95 (0.00%)	
occurrences (all)	43	23	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 November 2008	Restriction of study population to patients with confirmed KRAS wild-type mCRC. Patients under treatment who had confirmed KRAS mutation status had to stop study treatment.
18 June 2009	Change of cetuximab IMP to labeled marketing drug supply

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.

Due to the substantial amendment that only confirmed KRAS wild-type patients were allowed in future to proceed study medication recruitment process was slowed down and patients under treatment with KRAS mutated tumor were withdrawn from study.

Notes: