Clinical trial results:
A Phase IIA Open Label, Adaptive, Randomized Clinical Trial of Dalotuzumab (MK-0646) Treatment in Combination with Irinotecan Versus Cetuximab and Irinotecan for Patients with Metastatic Rectal Cancers (mRC) Expressing High IGF-1/Low IGF-2 Levels

The data reported in v1 is not correct and has been removed from public view

Summary

EudraCT number	2012-000317-36
Trial protocol	ES SE GB BE DK
Global end of trial date	09 December 2014

Results information

Result version number	v2 (current)
This version publication date	29 April 2016
First version publication date	10 February 2016
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	0646-025

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01609231
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com

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	09 December 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 December 2014
Global end of trial reached?	Yes
Global end of trial date	09 December 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of this adaptive trial is to compare the progression-free survival of participants with metastatic rectal carcinoma when treated with dalotuzumab + irinotecan therapy relative to participants treated with cetuximab + irinotecan. The primary study hypothesis is that administration of dalotuzumab in combination with irinotecan to participants with wild-type KRAS metastatic rectal carcinoma with high IGF-1/low IGF-2 expression levels improves progression-free survival compared to participants treated with cetuximab in combination with irinotecan.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 July 2012
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	Korea, Republic of: 5
Country: Number of subjects enrolled	New Zealand: 2
Country: Number of subjects enrolled	Norway: 1
Country: Number of subjects enrolled	Spain: 3
Worldwide total number of subjects	11
EEA total number of subjects	4

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)	5
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants with metastatic rectal carcinoma with high levels of tumor IGF-1/low levels of tumor IGF-2 and a wild type KRAS (wtKRAS) genotype, who experience disease progression on, or following, oxaliplatin and irinotecan–based chemotherapy and eligible to receive EGFR inhibitors.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Dalotuzumab + irinotecan

Arm description:

Participants receive irinotecan intravenously (IV), 180 mg/m^2 once every two weeks + dalotuzumab IV, 10 mg/kg once weekly

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

Dosage and administration details:

IV administration

Investigational medicinal product name	dalotuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

IV adminisration

Arm title	Cetuximab + irinotecan

Arm description:

Participants receive cetuximab IV, initial dose of 400 mg/m^2 and then 250 mg/m^2 IV weekly + irinotecan IV, 180 mg/m^2 once every two weeks

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

Dosage and administration details:

IV administration

Investigational medicinal product name	cetuximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

IV administration

Number of subjects in period 1	Dalotuzumab + irinotecan	Cetuximab + irinotecan
Started	6	5
Completed	3	2
Not completed	3	3
Adverse event, serious fatal	1	1
Physician decision	1	-
Consent withdrawn by subject	1	-
Adverse event, non-fatal	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Dalotuzumab + irinotecan
Reporting group description:	
Participants receive irinotecan intravenously (IV), 180 mg/m^2 once every two weeks + dalotuzumab IV, 10 mg/kg once weekly	
Reporting group title	Cetuximab + irinotecan
Reporting group description:	
Participants receive cetuximab IV, initial dose of 400 mg/m^2 and then 250 mg/m^2 IV weekly + irinotecan IV, 180 mg/m^2 once every two weeks	

Reporting group values	Dalotuzumab + irinotecan	Cetuximab + irinotecan	Total
Number of subjects	6	5	11
Age Categorical Units: Subjects			
Adults (18-64 years)	4	1	5
From 65-84 years	2	4	6
Age Continuous Units: years			
arithmetic mean	57.2	64.6	
standard deviation	± 13.8	± 9.9	-
Gender Categorical Units: Subjects			
Female	3	2	5
Male	3	3	6

End points

End points reporting groups

Reporting group title	Dalotuzumab + irinotecan
Reporting group description:	
Participants receive irinotecan intravenously (IV), 180 mg/m^2 once every two weeks + dalotuzumab IV, 10 mg/kg once weekly	
Reporting group title	Cetuximab + irinotecan
Reporting group description:	
Participants receive cetuximab IV, initial dose of 400 mg/m^2 and then 250 mg/m^2 IV weekly + irinotecan IV, 180 mg/m^2 once every two weeks	

Primary: Progression-free Survival (PFS)

End point title	Progression-free Survival (PFS)[1]
End point description:	
PFS is a measure of the amount of time from randomization to the first documented disease progression (assessed by an independent radiology review Committee) or participant death, whichever occurs first	
End point type	Primary
End point timeframe:	
From randomization (Cycle 1 Day 1) to the first documented disease progression or death due to any cause, whichever occurs first (up to 3 years)	

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: insufficient data were collected for this analysis

End point values	Dalotuzumab + irinotecan	Cetuximab + irinotecan		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: Months				
median (confidence interval 95%)	(to)	(to)		

Notes:

[2] - Due to early termination of study, insufficient data were collected for this endpoint.

[3] - Due to early termination of study, insufficient data were collected for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)
End point description:	
ORR will be based on the number of participants achieving a complete response (CR) or partial response (PR) during the course of the study using enhanced Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1). Confirmation of response is not required.	
End point type	Secondary
End point timeframe:	
From randomization (Cycle 1 Day 1) to the first documented disease progression or death due to any cause, whichever occurs first (up to 3 years)	

End point values	Dalotuzumab + irinotecan	Cetuximab + irinotecan		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[4]	0[5]		
Units: Percentage of Participants				

Notes:

[4] - Due to early termination of study, insufficient data were collected for this endpoint.

[5] - Due to early termination of study, insufficient data were collected for this endpoint.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From screening through 30 days following the last dose of study treatment.

Adverse event reporting additional description:

AE additional description

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Cetuximab + irinotecan

Reporting group description: -

Reporting group title	Dalotuzumab + irinotecan

Reporting group description: -

Serious adverse events	Cetuximab + irinotecan	Dalotuzumab + irinotecan	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 5 (80.00%)	1 / 6 (16.67%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	1	0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastrointestinal disorders			
Ileus			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			

Dyspnoea			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bursitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 6 (16.67%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Septic shock			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cetuximab + irinotecan	Dalotuzumab + irinotecan	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	6 / 6 (100.00%)	
Vascular disorders			

Haematoma			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 5 (20.00%)	2 / 6 (33.33%)	
occurrences (all)	4	6	
Catheter site pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	2 / 5 (40.00%)	1 / 6 (16.67%)	
occurrences (all)	3	2	
Mucosal inflammation			
subjects affected / exposed	2 / 5 (40.00%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Oedema peripheral			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	2	
Pyrexia			
subjects affected / exposed	0 / 5 (0.00%)	2 / 6 (33.33%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Cough			
subjects affected / exposed	1 / 5 (20.00%)	2 / 6 (33.33%)	
occurrences (all)	1	5	
Dyspnoea			
subjects affected / exposed	2 / 5 (40.00%)	3 / 6 (50.00%)	
occurrences (all)	2	5	
Epistaxis			

subjects affected / exposed	1 / 5 (20.00%)	1 / 6 (16.67%)	
occurrences (all)	1	2	
Hypoxia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Laryngeal pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Productive cough			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Rhinorrhoea			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	2	
Throat irritation			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Investigations			
Haemoglobin decreased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Neutrophil count decreased			
subjects affected / exposed	1 / 5 (20.00%)	2 / 6 (33.33%)	
occurrences (all)	3	2	
Platelet count decreased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Protein urine present			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Weight decreased			

subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Circadian rhythm sleep disorder			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	2	
Dysgeusia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Headache			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	2	
Neuropathy peripheral			
subjects affected / exposed	2 / 5 (40.00%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 5 (40.00%)	2 / 6 (33.33%)	
occurrences (all)	3	2	
Lymphadenopathy			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Neutropenia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 6 (16.67%)	
occurrences (all)	1	2	
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	2	
Vertigo			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Eye disorders			

Blepharitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Conjunctivitis allergic			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Eye pruritus			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Abdominal pain			
subjects affected / exposed	2 / 5 (40.00%)	3 / 6 (50.00%)	
occurrences (all)	2	4	
Abdominal pain upper			
subjects affected / exposed	1 / 5 (20.00%)	1 / 6 (16.67%)	
occurrences (all)	2	1	
Cheilitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	3 / 5 (60.00%)	1 / 6 (16.67%)	
occurrences (all)	4	1	
Diarrhoea			
subjects affected / exposed	4 / 5 (80.00%)	6 / 6 (100.00%)	
occurrences (all)	18	23	
Dry mouth			
subjects affected / exposed	2 / 5 (40.00%)	1 / 6 (16.67%)	
occurrences (all)	3	6	
Epigastric discomfort			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			

subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Frequent bowel movements			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Gingival oedema			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Haematochezia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	2	
Nausea			
subjects affected / exposed	4 / 5 (80.00%)	3 / 6 (50.00%)	
occurrences (all)	9	7	
Oral pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Stomatitis			
subjects affected / exposed	3 / 5 (60.00%)	0 / 6 (0.00%)	
occurrences (all)	3	0	
Toothache			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	2 / 5 (40.00%)	3 / 6 (50.00%)	
occurrences (all)	5	6	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Alopecia			
subjects affected / exposed	2 / 5 (40.00%)	2 / 6 (33.33%)	
occurrences (all)	2	3	
Dermatitis acneiform			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	

Dry skin			
subjects affected / exposed	2 / 5 (40.00%)	0 / 6 (0.00%)	
occurrences (all)	3	0	
Nail disorder			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	2 / 5 (40.00%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Rash			
subjects affected / exposed	4 / 5 (80.00%)	1 / 6 (16.67%)	
occurrences (all)	6	1	
Skin fissures			
subjects affected / exposed	3 / 5 (60.00%)	1 / 6 (16.67%)	
occurrences (all)	6	1	
Skin lesion			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Skin mass			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	2 / 5 (40.00%)	0 / 6 (0.00%)	
occurrences (all)	3	0	
Polyuria			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Renal failure acute			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 6 (16.67%)	
occurrences (all)	1	2	
Back pain			
subjects affected / exposed	1 / 5 (20.00%)	3 / 6 (50.00%)	
occurrences (all)	1	4	
Bone erosion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Joint swelling			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Muscular weakness			
subjects affected / exposed	1 / 5 (20.00%)	1 / 6 (16.67%)	
occurrences (all)	3	1	
Musculoskeletal discomfort			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Musculoskeletal pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	3	
Pain in extremity			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	4	
Infections and infestations			
Bacteriuria			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	2	
Candida infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Cellulitis			

subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Fungal skin infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Gingival abscess			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	0 / 5 (0.00%)	2 / 6 (33.33%)	
occurrences (all)	0	3	
Paronychia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	3	0	
Rhinitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Skin infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	3	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 5 (80.00%)	4 / 6 (66.67%)	
occurrences (all)	5	16	
Dehydration			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Hyperglycaemia			
subjects affected / exposed	0 / 5 (0.00%)	2 / 6 (33.33%)	
occurrences (all)	0	3	
Hypoalbuminaemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	

Hypocalcaemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Hypokalaemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 December 2012	Amendment 3 was done in response to differences in standards for management of cetuximab and irinotecan pre-medications between the United States and other countries – flexible language was added to allow Investigators to meet institutional and Regulatory guidelines. Product inserts were removed from the protocol to avoid confusion and allow each country to use their country-specific circular.
28 February 2013	Amendment 4 added an additional interim analysis to evaluate tumor response at 6 weeks; the effect of treatment on changes in tumor volume at 6 weeks was to be the basis for a decision on whether or not to continue to the next planned interim analysis or to stop the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
28 October 2013	The study did not meet target enrollment and was terminated for business reasons.	-

Notes:

Limitations and caveats

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

The study did not meet target enrollment and was terminated for business reasons; insufficient data were collected for efficacy analyses. Safety data are reported.

Notes: