Clinical trial results:
Phase II trial to evaluate the efficacy and safety of chemoradiotherapy with 5-fluorouracil, mitomycin C and panitumumab as a treatment for squamous cell carcinoma of the anal canal

Summary

EudraCT number	2010-018430-48
Trial protocol	ES
Global end of trial date	16 April 2019

Results information

Result version number	v1 (current)
This version publication date	31 July 2019
First version publication date	31 July 2019

Trial information

Trial identification

Sponsor protocol code	GEMCAD-09-02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01285778
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Grupo Español Multidisciplinar en Cáncer Digestivo (GEMCAD)
Sponsor organisation address	Pau Alsina, 64-68, esc. B, entlo. 5ª, Barcelona, Spain, 08024
Public contact	Dr. Carlos Fernández Martos , Grupo Español Multidisciplinar en Cáncer Digestivo (GEMCAD), 0034 934344412, secretaria@gemcad.org
Scientific contact	Dr. Carlos Fernández Martos , Grupo Español Multidisciplinar en Cáncer Digestivo (GEMCAD), 0034 934344412, secretaria@gemcad.org

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	26 April 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 January 2017
Global end of trial reached?	Yes
Global end of trial date	16 April 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To estimate the three-year disease-free survival rate in patients treated with 5-FU, mytomicin C and panitumumab concurrently with radiation therapy as treatment for squamous cell carcinoma of the anal canal (SCCAC).

Protection of trial subjects:

For subjects who experienced unacceptable toxicity while in the study, one or more doses of panitumumab were suspended, reduced or delayed. Once the toxicity was solved, a limited number of attempts were made to re-increase the reduced doses of panitumumab. Escalations of doses higher than the initial dose of 6.0 mg / kg were not allowed.

Background therapy:

None.

Evidence for comparator:

Chemoradiotherapy with 5-FU and mitomycin C is the standard of care in Europe and U.S for the SCCAC. Panitumumab has been effective in other tumors and anti-EGFR treatment has demonstrated clinical activity in a single report of a refractory patient with SCCAC.

Actual start date of recruitment	24 January 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 58
Worldwide total number of subjects	58
EEA total number of subjects	58

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)	41
From 65 to 84 years	17
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

58 patients were included in this study. All of them were included in the ITT, PP and safety populations. This national study included patients from 25 Spanish centers.

Pre-assignment

Screening details:

Key inclusion criteria: Male or female ≥18 years with histologically or cytologically confirmed SCACC; T2-T4 stage and any N stage (pelvic or inguinal) determined radiologically by MRI; ECOG performance status 0 to 2. All patients met the inclusion criteria.

Period 1

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

Blinding implementation details:

Not applicable.

Arms

Arm title	Treatment

Arm description:

Patients received treatment with panitumumab (Vectibix®, Amgen) 6 mg/kg intravenously (IV) on day 1 and every 2 weeks for 8 weeks. Panitumumab treatment was followed by 5-FU 1 000 mg/day by continuous IV infusion on days 1-4 and 29-32, and mitomycin C 10 mg/m2 IV on days 1 and 29. Radiotherapy was given on day 1-37 to a total dose of 45 Gy (1.8 Gy/fraction, 5 fractions per week) to the primary tumour and mesorectal, iliac and inguinal lymph nodes, plus a boost dose of 10-15 Gy to the primary tumour and affected lymph nodes.

Arm type	Experimental
Investigational medicinal product name	Panitumumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Panitumumab was administered by i.v. infusion. on day 1 and every 2 weeks for 8 weeks. The dose of panitumumab was 6 mg / kg. The total dose could be rounded up or down by no more than 10 mg. The dose of panitumumab was calculated from the subject's actual body weight at baseline (ie, cycle 1) and was not recalculated unless the changes in actual body weight were at least 10% from baseline. Panitumumab was diluted in a minimum of 100 mL of 0.9% sodium chloride apyrogenic solution, according to the USP / PhEur / JP (normal saline, provided by the center). The maximum concentration of the diluted solution that was administered by infusion should not exceed 10 mg / mL; if necessary, the volume of normal saline should be increased to 150 mL.

Investigational medicinal product name	Mitomycin C
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients received treatment with panitumumab (Vectibix®, Amgen) 6 mg/kg intravenously (IV) on day 1 and every 2 weeks for 8 weeks. Panitumumab treatment was followed by 5-FU 1 000 mg/day by continuous IV infusion on days 1-4 and 29-32, and mitomycin C 10 mg/m2 IV on days 1 and 29.

Investigational medicinal product name	5-fluorouracil (5-FU)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients received treatment with panitumumab (Vectibix®, Amgen) 6 mg/kg intravenously (IV) on day 1 and every 2 weeks for 8 weeks. Panitumumab treatment was followed by 5-FU 1 000 mg/day by continuous IV infusion on days 1-4 and 29-32, and mitomycin C 10 mg/m2 IV on days 1 and 29.

Investigational medicinal product name	Radiotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Radiotherapy was administered on day 1-37 to a total dose of 45 Gy (1.8 Gy/fraction, 5 fractions per week) to the primary tumour and mesorectal, iliac and inguinal lymph nodes, plus a boost dose of 10-15 Gy to the primary tumour and affected lymph nodes.

Number of subjects in period 1	Treatment
Started	58
Completed	58

Baseline characteristics

Reporting groups	
Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	58	58	
Age categorical			
Adults aged between 33 and 83 years.			
Units: Subjects			
Adults (18-64 years)	41	41	
From 65-84 years	17	17	
Age continuous			
Units: years			
median	59.2		
inter-quartile range (Q1-Q3)	49.9 to 66.0	-	
Gender categorical			
Adult men and women			
Units: Subjects			
Female	31	31	
Male	27	27	
ECOG performance status			
Units: Subjects			
ECOG 0	24	24	
ECOG 1	33	33	
ECOG 2	1	1	
TNM stage			
Units: Subjects			
TNM stage I	0	0	
TNM stage II	17	17	
TNM stage IIIA	12	12	
TNM stage IIIB	27	27	
TNM stage NE	2	2	
HIV positive			
13 patients for the HIV results were not evaluated.			
Units: Subjects			
HIV positive	4	4	
HIV negative	41	41	
Not recorded	13	13	
HPV positive			
12 patients for the HPV results were not evaluated.			
Units: Subjects			
HPV positive	39	39	
HPV negative	7	7	
Not recorded	12	12	
Etnicity			
Units: Subjects			

Caucasian	57	57	
Other	1	1	

End points

End points reporting groups

Reporting group title	Treatment

Reporting group description:

Patients received treatment with panitumumab (Vectibix®, Amgen) 6 mg/kg intravenously (IV) on day 1 and every 2 weeks for 8 weeks. Panitumumab treatment was followed by 5-FU 1 000 mg/day by continuous IV infusion on days 1-4 and 29-32, and mitomycin C 10 mg/m2 IV on days 1 and 29. Radiotherapy was given on day 1-37 to a total dose of 45 Gy (1.8 Gy/fraction, 5 fractions per week) to the primary tumour and mesorectal, iliac and inguinal lymph nodes, plus a boost dose of 10-15 Gy to the primary tumour and affected lymph nodes.

Primary: 3-year disease-free survival (DFS %)

End point title	3-year disease-free survival (DFS %)[1]

End point description:

Disease free survival was defined as number of months between the first treatment dose until the first treatment failure (defined as disease progression by MRI or CT, persistence of disease confirmed by biopsy performed at least 6 months after end of treatment, rescue surgery/colostomy by progression or death by progression).

End point type	Primary

End point timeframe:

Percentage of subjects who are still alive and without disease after 3 years of follow-up.

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: No statistical analysis was performed. There was only one arm treatment.

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	58			
Units: percent				
number (confidence interval 95%)				
36 months	61.09 (47.13 to 72.40)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS %)

End point title	Progression Free Survival (PFS %)

End point description:

Progression free survival was defined as the number of months between the first treatment dose until progression, rescue surgery/colostomy due to progression or death.

End point type	Secondary

End point timeframe:

Time from the 1st dose of treatment to 3 years of progression.

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	58			
Units: percent				
number (confidence interval 95%)				
36 months	57.54 (43.64 to 69.19)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS %)

End point title	Overall survival (OS %)

End point description:

Overall survival was defined as number of months between first treatment dose and death for any reason.

End point type	Secondary

End point timeframe:

Overall survival at 3 years.

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	58			
Units: percent				
number (confidence interval 95%)				
36 months	78.4 (65.1 to 87.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Colostomy free survival (CFS %)

End point title	Colostomy free survival (CFS %)

End point description:

Colostomy free survival rate was defined as the number of patients alive and without a colostomy.

End point type	Secondary

End point timeframe:

Percentage of subjects who are still alive and without colostomy after 2 years of follow-up.

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	58			
Units: percent				
number (confidence interval 95%)				
24 months	68.11 (54.24 to 78.58)			

Statistical analyses

No statistical analyses for this end point

Secondary: Locoregional failure (LRF %) free rate

End point title	Locoregional failure (LRF %) free rate

End point description:

LRF was defined as relapse of disease in the anal canal and/or regional organs and/or regional lymph nodes.

End point type	Secondary

End point timeframe:

Percentage of subjects who continue without local-regional relapses after 3 years of follow-up.

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	58			
Units: percent				
number (confidence interval 95%)				
36 months	64.77 (50.87 to 75.65)			

Statistical analyses

No statistical analyses for this end point

Secondary: Distant failure free rate (%)

End point title	Distant failure free rate (%)

End point description:

LRF was defined as relapse of disease in the anal canal and/or regional organs and/or regional lymph nodes. All other relapses were considered distant failures.

End point type	Secondary

End point timeframe:

Percentage of subjects who continue without relapses at distance after 3 years of follow-up.

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	58			
Units: percent				
number (confidence interval 95%)				
36 months	92.98 (82.37 to 97.31)			

Statistical analyses

No statistical analyses for this end point

Secondary: Complete response (CR) rate

End point title	Complete response (CR) rate

End point description:

Percentage of subjects who have reached a clinical and radiological CR. Response was evaluated clinically or radiologically according to Response Evaluation Criteria in Solid Tumours (RECIST) criteria (version 1.1).

End point type	Secondary

End point timeframe:

Patients who have reached at some point a clinical and/or radiological CR during the study.

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	58			
Units: percent				
number (confidence interval 95%)	81.0 (69.8 to 92.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Recurrence free survival (CFS %))

End point title	Recurrence free survival (CFS %))

End point description:

Recurrence free survival was defined as number of months between the first CR to the treatment until the first treatment failure (disease progression analysed by MRI or TC, rescue surgery/colostomy due to progression or death due to progression).

End point type	Secondary

End point timeframe:

CFS at 2 years.

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	58			
Units: percent				
number (confidence interval 95%)				
24 months	72.75 (56.20 to 83.89)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Analysis of duplication

End point title	Analysis of duplication

End point description:

Evaluation of the predictive molecular markers of response: the presence of duplications in 23 different genes in 27 patients with available samples.

End point type	Other pre-specified

End point timeframe:

During the study

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	27			
Units: frequency				
number (not applicable)				
EGFR	26			
KRAS	37			
BRAF	0			
PIK3CA	85			
PTEN	26			
BRCA1	4			
BRCA2	22			
ERCC1	48			
ERCC6	4			
ERCC3	4			
ERCC4	26			
ERCC2	37			
ERCC8	33			
ERCC5	19			

XRCC1	30			
XRCC2	59			
XRCC3	4			
XRCC5	4			
XRCC6	26			
XRCC4	30			
CCNA2 (cyclin a)	19			
TP53	15			
MDM2	30			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Analysis of deletions

End point title	Analysis of deletions

End point description:

Evaluation of the predictive molecular markers of response: the presence of deletions in 23 different genes in 27 patients with available samples.

End point type	Other pre-specified

End point timeframe:

During the study

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	27			
Units: frequency				
number (not applicable)				
EGFR	7			
KRAS	0			
BRAF	15			
PIK3CA	0			
PTEN	15			
BRCA1	59			
BRCA2	33			
ERCC1	4			
ERCC6	74			
ERCC3	30			
ERCC4	7			
ERCC2	7			
ERCC8	15			
ERCC5	22			
XRCC1	0			
XRCC2	7			
XRCC3	33			
XRCC5	37			

XRCC6	7			
XRCC4	15			
CCNA2 (cyclin a)	19			
TP53	48			
MDM2	7			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Analysis of single nucleotide polymorphisms (SNP)

End point title	Analysis of single nucleotide polymorphisms (SNP)

End point description:

Evaluation of the predictive molecular markers of response: the presence of SNP in 23 different genes in 27 patients with available samples.

End point type	Other pre-specified

End point timeframe:

During the study

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	58			
Units: frequency				
number (not applicable)				
EGFR	0			
KRAS	0			
BRAF	4			
PIK3CA	33			
PTEN	4			
BRCA1	15			
BRCA2	7			
ERCC1	0			
ERCC6	7			
ERCC3	7			
ERCC4	4			
ERCC2	4			
ERCC8	0			
ERCC5	4			
XRCC1	0			
XRCC2	0			
XRCC3	0			
XRCC5	0			
XRCC6	4			
XRCC4	7			
CCNA2 (cyclin a)	0			
TP53	4			

MDM2	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The medically significant AEs that the investigator or the promoter considered related to the product under investigation were monitored until their resolution or until stabilization.

Adverse event reporting additional description:

SAEs were collected and reported within 1 working day of the discovery or notification of the event if it appeared > 30 days after the last dose of the investigational product or after the end of the study and if it was believed that it was possibly related to the product under investigation.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Treatment

Reporting group description:

Patients received treatment with: 1,000 mg2 of 5-FU on days 1-4 and 29-32; 10 mg / m2 of mitomycin C on days 1 and 29; 6 mg / m2 of panitumumab on day 1 and every 2 weeks for 8 weeks; Radiotherapy: 45 Gy (1.8 Gy per fraction) in the regional and inguinal lymph nodes and the primary tumor, and then a 10-15 Gy boost in the primary tumor and affected lymph nodes.

Serious adverse events	Treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 58 (41.38%)		
number of deaths (all causes)	13		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Radiation skin injury			
subjects affected / exposed	4 / 58 (6.90%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Weight decreased			

subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mucosal inflammation			
subjects affected / exposed	2 / 58 (3.45%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Platelet count decreased			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	4 / 58 (6.90%)		
occurrences causally related to treatment / all	3 / 5		
deaths causally related to treatment / all	0 / 0		
Pancytopenia			
subjects affected / exposed	2 / 58 (3.45%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			

subjects affected / exposed	4 / 58 (6.90%)			
occurrences causally related to treatment / all	2 / 4			
deaths causally related to treatment / all	0 / 0			
Enteritis				
subjects affected / exposed	2 / 58 (3.45%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Proctalgia				
subjects affected / exposed	3 / 58 (5.17%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Subileus				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Dermatitis				
subjects affected / exposed	2 / 58 (3.45%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Osteoarthritis				
subjects affected / exposed	1 / 58 (1.72%)			
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	1 / 58 (1.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Pneumonia			
subjects affected / exposed	2 / 58 (3.45%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Treatment		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	58 / 58 (100.00%)		
Injury, poisoning and procedural complications			
Radiation skin injury			
subjects affected / exposed	38 / 58 (65.52%)		
occurrences (all)	110		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	6 / 58 (10.34%)		
occurrences (all)	7		
Blood and lymphatic system disorders			
Platelet count decreased			
subjects affected / exposed	7 / 58 (12.07%)		
occurrences (all)	12		
Anaemia			
subjects affected / exposed	16 / 58 (27.59%)		
occurrences (all)	35		
Leukopenia			
subjects affected / exposed	11 / 58 (18.97%)		
occurrences (all)	13		
Lymphopenia			
subjects affected / exposed	12 / 58 (20.69%)		
occurrences (all)	26		
Neutropenia			
subjects affected / exposed	25 / 58 (43.10%)		
occurrences (all)	46		
Febrile neutropenia			

subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	9		
Thrombocytopenia			
subjects affected / exposed	14 / 58 (24.14%)		
occurrences (all)	19		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	33 / 58 (56.90%)		
occurrences (all)	54		
Pain			
subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	6		
Mucosal inflammation			
subjects affected / exposed	25 / 58 (43.10%)		
occurrences (all)	38		
Pyrexia			
subjects affected / exposed	10 / 58 (17.24%)		
occurrences (all)	13		
Xerosis			
subjects affected / exposed	4 / 58 (6.90%)		
occurrences (all)	6		
Oedema peripheral			
subjects affected / exposed	4 / 58 (6.90%)		
occurrences (all)	5		
Eye disorders			
Conjunctivitis			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	3		
Reproductive system and breast disorders			
Perineal pain			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	4		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	44 / 58 (75.86%)		
occurrences (all)	90		

Abdominal pain				
subjects affected / exposed	14 / 58 (24.14%)			
occurrences (all)	18			
Abdominal pain upper				
subjects affected / exposed	5 / 58 (8.62%)			
occurrences (all)	5			
Enteritis				
subjects affected / exposed	4 / 58 (6.90%)			
occurrences (all)	5			
Perianal erythema				
subjects affected / exposed	3 / 58 (5.17%)			
occurrences (all)	8			
Stomatitis				
subjects affected / exposed	10 / 58 (17.24%)			
occurrences (all)	18			
Constipation				
subjects affected / exposed	12 / 58 (20.69%)			
occurrences (all)	14			
Rectal haemorrhage				
subjects affected / exposed	4 / 58 (6.90%)			
occurrences (all)	4			
Haemorrhoids				
subjects affected / exposed	3 / 58 (5.17%)			
occurrences (all)	5			
Anal incontinence				
subjects affected / exposed	3 / 58 (5.17%)			
occurrences (all)	3			
Anal inflammation				
subjects affected / exposed	4 / 58 (6.90%)			
occurrences (all)	9			
Anorectal discomfort				
subjects affected / exposed	3 / 58 (5.17%)			
occurrences (all)	4			
Nausea				
subjects affected / exposed	18 / 58 (31.03%)			
occurrences (all)	22			

Odynophagia subjects affected / exposed occurrences (all)	4 / 58 (6.90%) 4			
Proctalgia subjects affected / exposed occurrences (all)	20 / 58 (34.48%) 26			
Proctitis subjects affected / exposed occurrences (all)	5 / 58 (8.62%) 8			
Rectal tenesmus subjects affected / exposed occurrences (all)	6 / 58 (10.34%) 6			
Vomiting subjects affected / exposed occurrences (all)	13 / 58 (22.41%) 17			
Skin and subcutaneous tissue disorders				
Acne subjects affected / exposed occurrences (all)	6 / 58 (10.34%) 14			
Alopecia subjects affected / exposed occurrences (all)	4 / 58 (6.90%) 4			
Dermatitis subjects affected / exposed occurrences (all)	9 / 58 (15.52%) 18			
Dermatitis acneiform subjects affected / exposed occurrences (all)	13 / 58 (22.41%) 20			
Erythema subjects affected / exposed occurrences (all)	4 / 58 (6.90%) 7			
Rash subjects affected / exposed occurrences (all)	31 / 58 (53.45%) 52			
Skin fissures				

subjects affected / exposed occurrences (all) Dry skin subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all)	3 / 58 (5.17%) 5 5 / 58 (8.62%) 10 3 / 58 (5.17%) 4		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	 4 / 58 (6.90%) 4		
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	 11 / 58 (18.97%) 14		
Infections and infestations Oral candidiasis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) Pneumonia subjects affected / exposed occurrences (all)	 4 / 58 (6.90%) 4 3 / 58 (5.17%) 3 4 / 58 (6.90%) 4		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) Hypokalaemia subjects affected / exposed occurrences (all) Hypomagnesaemia subjects affected / exposed occurrences (all)	 16 / 58 (27.59%) 23 7 / 58 (12.07%) 7 15 / 58 (25.86%) 17		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 March 2010	Through this amendment, the changes suggested by the Clinical Research Ethics Committees in the protocol were: the Subject Information Sheet, the Informed Consent Form, the Subject Information Sheet and the Informed Consent form of the optional study of molecular predictors. The changes to the protocol were as follows: the amount of panitumumab per vial was specified; and appendix E (panitumumab pharmaceutical guide) was modified in order to facilitate its comprehension.
25 January 2011	Through this amendment several typographical errors were amended in the protocol in order to facilitate its comprehension.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported