Clinical trial results:
Panitumumab in combination with cisplatin/gemcitabine chemotherapy in patients with cholangiocarcinomas - a randomized clinical phase II study - PiCCA Study

Summary

EudraCT number	2010-018850-11
Trial protocol	DE
Global end of trial date	04 December 2015

Results information

Result version number	v1 (current)
This version publication date	02 January 2025
First version publication date	02 January 2025

Trial information

Trial identification

Sponsor protocol code	MHH_CCA_AG54

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01320254
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hannover Medical School
Sponsor organisation address	Carl-Neuberg-Str. 1, Hannover, Germany, 30625
Public contact	Stabsstelle Zentrum für Klinische Studien, Hannover Medical School, EudraCT@mh-hannover.de
Scientific contact	Stabsstelle Zentrum für Klinische Studien, Hannover Medical School, EudraCT@mh-hannover.de

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	13 October 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 December 2015
Global end of trial reached?	Yes
Global end of trial date	04 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy of panitumumab plus the cisplatin/gemcitabine combination chemotherapy in k-ras wildtype in patients with cholangiocarcinoma / gallbladder carcinoma, compared to the historical data for the same chemotherapy, which are verified by a randomised control group without the antibody.

Protection of trial subjects:

The clinical trial was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki and with the standards of International Conference on Harmonisation (ICH) Good Clinical Practice (GCP). A continuous risk assessment was performed during the study.

Background therapy:

Cisplatin and Gemcitabine are considered as chemotherapy backbone medication, as well as reference therapy.
Cisplatin 25 mg/m² day 1 and day 8 / q3w
Gemcitabine 1000mg/m² day 1 and day 8 / q3w

Evidence for comparator:

Several phase II trials in CCA with a variety of cytostatic drugs incorporated have shown, that two-drug chemotherapy combinations typically lead to response rates of about 30%, ranging from 20% to 45%. With gemcitabine/cisplatin a median progression-free survival (PFS) of 8.5 months was achieved in a randomized phase III trial. This corresponds to a PFS rate of 61% after 6 months.
Data on metastatic colorectal cancer suggest, that panitumumab is especially active in patients with KRAS wildtype tumors, which comprise about 60% of all colorectal carcinomas. A rather similar proportion has been described for CCA. However, the role of KRAS as a predictive marker for anti-EGFR-therapy in patients with cholangiocarcinomas and gallbladder-carcinomas is unknown.

Actual start date of recruitment	13 April 2011
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: 90
Worldwide total number of subjects	90
EEA total number of subjects	90

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)	75
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited at 16 different centers all based in Germany. Eligibility was determined based upon the inclusion and exclusion criteria.

Pre-assignment

Screening details:

Eligibility was determined based upon the inclusion and exclusion criteria.

Period 1

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

Blinding implementation details:

not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

cisplatin/gemcitabine+panitumumab

Arm type	Experimental
Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatin 25 mg/m² day 1 and day 8 / q3w

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine 1000mg/m² day 1 and day 8 / q3w

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

Dosage and administration details:

9mg/kg BW q3w

Arm title	Arm B

Arm description:

cisplatin/gemcitabine

Arm type	Active comparator

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatin 25 mg/m² day 1 and day 8 / q3w

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine 1000mg/m² day 1 and day 8 / q3w

Number of subjects in period 1	Arm A	Arm B
Started	62	28
Completed	17	9
Not completed	45	19
died during follow-up	45	19

Baseline characteristics

Reporting groups	
Reporting group title	Arm A
Reporting group description: cisplatin/gemcitabine+panitumumab	
Reporting group title	Arm B
Reporting group description: cisplatin/gemcitabine	

Reporting group values	Arm A	Arm B	Total
Number of subjects	62	28	90
Age categorical Units: Subjects			
<=40 Jahre	1	1	2
41-50 Jahre	9	5	14
51-60 Jahre	15	10	25
61-70 Jahre	24	10	34
>70 Jahre	13	2	15
Age continuous Units: years			
arithmetic mean	61.6	58.5	
standard deviation	± 11	± 10.5	-
Gender categorical Units: Subjects			
Female	26	14	40
Male	36	14	50
localisation of tumor Units: Subjects			
Cholangicarcinoma	50	25	75
gall bladder carcinoma	12	3	15

End points

End points reporting groups	
Reporting group title	Arm A
Reporting group description: cisplatin/gemcitabine+panitumumab	
Reporting group title	Arm B
Reporting group description: cisplatin/gemcitabine	

Primary: progression free survival rate after 6 months	
End point title	progression free survival rate after 6 months
End point description: The primary endpoint of the study is the progression-free survival rate after 6 months, based on the ITT population. The progression-free survival rate at six months is defined as the number of patients recorded to be free of progression (according to RECIST) at this time point, divided by the number of patients randomized to the respective arm	
End point type	Primary
End point timeframe: 6 months follow-up	

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	26		
Units: progression free survival rate				
number (confidence interval 95%)	54 (41 to 67)	73 (52 to 88)		

Statistical analyses

Statistical analysis title	Progression free survivalt at 6 months
Statistical analysis description: difference of progression free survival at 6 months between treatment and comparison group	
Comparison groups	Arm A v Arm B
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.319
Method	Fisher exact

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Reporting of (S)AEs commences at subject enrolment into the study until the EOT Visit or 30 days after the last dose of IMP.

Adverse event reporting additional description:

Evaluation of safety criteria is covered by documentation and reporting of adverse events and serious adverse events throughout study therapy, according to NCI CTCAE.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	3.0

Reporting groups

Reporting group title	ArmA

Reporting group description:

Cisplatin/Gemcitabin + Panitumumab

Reporting group title	ArmB

Reporting group description:

Cisplatin/Gemcitabin

Serious adverse events	ArmA	ArmB	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 59 (11.86%)	0 / 26 (0.00%)	
number of deaths (all causes)	7	0	
number of deaths resulting from adverse events	7	0	
Cardiac disorders			
subcutaneous myocardial infarction			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatobiliary disorders			
Tumor progression			
subjects affected / exposed	6 / 59 (10.17%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 6	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	ArmA	ArmB	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	59 / 59 (100.00%)	26 / 26 (100.00%)	
Vascular disorders			
Flushing			
subjects affected / exposed	4 / 59 (6.78%)	3 / 26 (11.54%)	
occurrences (all)	4	3	
Hematoma			
subjects affected / exposed	4 / 59 (6.78%)	1 / 26 (3.85%)	
occurrences (all)	4	1	
Hypertension			
subjects affected / exposed	3 / 59 (5.08%)	2 / 26 (7.69%)	
occurrences (all)	3	2	
Hypotension			
subjects affected / exposed	5 / 59 (8.47%)	2 / 26 (7.69%)	
occurrences (all)	5	2	
Peripheral arterial ischemia			
subjects affected / exposed	2 / 59 (3.39%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Phlebitis			
subjects affected / exposed	0 / 59 (0.00%)	2 / 26 (7.69%)	
occurrences (all)	0	2	
Thrombosis/embolism (vascular accesss)			
subjects affected / exposed	0 / 59 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Thrombosis/thrombus/ embolism			
subjects affected / exposed	6 / 59 (10.17%)	5 / 26 (19.23%)	
occurrences (all)	6	5	
General disorders and administration site conditions			
Edema: head and neck			
subjects affected / exposed	1 / 59 (1.69%)	3 / 26 (11.54%)	
occurrences (all)	1	3	
Edema: limb			
subjects affected / exposed	13 / 59 (22.03%)	7 / 26 (26.92%)	
occurrences (all)	13	7	
Fatigue			

subjects affected / exposed	44 / 59 (74.58%)	21 / 26 (80.77%)	
occurrences (all)	44	21	
Fever			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Fever (any cause)			
subjects affected / exposed	16 / 59 (27.12%)	3 / 26 (11.54%)	
occurrences (all)	16	3	
Injection site reaction			
subjects affected / exposed	3 / 59 (5.08%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Mucositis			
subjects affected / exposed	28 / 59 (47.46%)	8 / 26 (30.77%)	
occurrences (all)	28	8	
Pain			
subjects affected / exposed	44 / 59 (74.58%)	21 / 26 (80.77%)	
occurrences (all)	44	21	
Rigors/chills			
subjects affected / exposed	2 / 59 (3.39%)	2 / 26 (7.69%)	
occurrences (all)	2	2	
SIRS			
subjects affected / exposed	4 / 59 (6.78%)	1 / 26 (3.85%)	
occurrences (all)	4	1	
Worsening of general condition			
subjects affected / exposed	3 / 59 (5.08%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Immune system disorders			
Allergic reaction			
subjects affected / exposed	4 / 59 (6.78%)	0 / 26 (0.00%)	
occurrences (all)	4	0	
Respiratory, thoracic and mediastinal disorders			
Airway obstruction			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Cough			

subjects affected / exposed	8 / 59 (13.56%)	1 / 26 (3.85%)	
occurrences (all)	8	1	
Dyspnea			
subjects affected / exposed	13 / 59 (22.03%)	4 / 26 (15.38%)	
occurrences (all)	13	4	
Hemorrhage pulmonary			
subjects affected / exposed	3 / 59 (5.08%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Pulmonary - Other			
subjects affected / exposed	0 / 59 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	6 / 59 (10.17%)	1 / 26 (3.85%)	
occurrences (all)	6	1	
Mood alteration			
subjects affected / exposed	4 / 59 (6.78%)	3 / 26 (11.54%)	
occurrences (all)	4	3	
Psychosis			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Investigations			
ALT			
subjects affected / exposed	0 / 59 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Alkaline phosphatase			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Bilirubin			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Creatinine			
subjects affected / exposed	2 / 59 (3.39%)	4 / 26 (15.38%)	
occurrences (all)	2	4	
GFR			

subjects affected / exposed	2 / 59 (3.39%)	2 / 26 (7.69%)	
occurrences (all)	2	2	
GGT			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Hemoglobin			
subjects affected / exposed	48 / 59 (81.36%)	22 / 26 (84.62%)	
occurrences (all)	48	22	
Metabolic/Lab - Other			
subjects affected / exposed	3 / 59 (5.08%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Neutrophils			
subjects affected / exposed	42 / 59 (71.19%)	24 / 26 (92.31%)	
occurrences (all)	42	24	
Weight gain			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Weight loss			
subjects affected / exposed	8 / 59 (13.56%)	1 / 26 (3.85%)	
occurrences (all)	8	1	
Injury, poisoning and procedural complications			
Burn			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Fracture			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Stricture, GI			
subjects affected / exposed	4 / 59 (6.78%)	1 / 26 (3.85%)	
occurrences (all)	4	1	
Wound complication, non-infectious			
subjects affected / exposed	3 / 59 (5.08%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Smoke intoxication			

subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Fall (stumbled)			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Cardiac General - Other			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Cardiac ischemia/infarction			
subjects affected / exposed	2 / 59 (3.39%)	2 / 26 (7.69%)	
occurrences (all)	2	2	
Supraventricular arrhythmia			
subjects affected / exposed	2 / 59 (3.39%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	8 / 59 (13.56%)	4 / 26 (15.38%)	
occurrences (all)	8	4	
Neurology - Other			
subjects affected / exposed	0 / 59 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Neuropathy-motor			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Neuropathy-sensory/ PNP			
subjects affected / exposed	16 / 59 (27.12%)	8 / 26 (30.77%)	
occurrences (all)	16	8	
Seizure			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Syncope (fainting)			
subjects affected / exposed	4 / 59 (6.78%)	1 / 26 (3.85%)	
occurrences (all)	4	1	
Taste alteration			

subjects affected / exposed	5 / 59 (8.47%)	4 / 26 (15.38%)	
occurrences (all)	5	4	
Tremor			
subjects affected / exposed	3 / 59 (5.08%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Blood and lymphatic system disorders			
Blood – Other (Specify)			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Febrile neutropenia			
subjects affected / exposed	4 / 59 (6.78%)	0 / 26 (0.00%)	
occurrences (all)	4	0	
Hemolysis			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Leukocytes			
subjects affected / exposed	43 / 59 (72.88%)	26 / 26 (100.00%)	
occurrences (all)	43	26	
Lymphopenia			
subjects affected / exposed	0 / 59 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Platelets			
subjects affected / exposed	42 / 59 (71.19%)	20 / 26 (76.92%)	
occurrences (all)	42	20	
Thrombotic microangiopathy			
subjects affected / exposed	0 / 59 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Hypokalaemia			
subjects affected / exposed	3 / 59 (5.08%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Ear and labyrinth disorders			
Auditory/Ear - Other (Specify)			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Hearing			

subjects affected / exposed	0 / 59 (0.00%)	3 / 26 (11.54%)	
occurrences (all)	0	3	
Tinnitus			
subjects affected / exposed	0 / 59 (0.00%)	2 / 26 (7.69%)	
occurrences (all)	0	2	
Eye disorders			
Dry eye			
subjects affected / exposed	2 / 59 (3.39%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Eyelid dysfunction			
subjects affected / exposed	2 / 59 (3.39%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Flashing lights			
subjects affected / exposed	0 / 59 (0.00%)	2 / 26 (7.69%)	
occurrences (all)	0	2	
Ocular - Other			
subjects affected / exposed	0 / 59 (0.00%)	2 / 26 (7.69%)	
occurrences (all)	0	2	
Ocular surface disease			
subjects affected / exposed	5 / 59 (8.47%)	0 / 26 (0.00%)	
occurrences (all)	5	0	
Vitreous hemorrhage			
subjects affected / exposed	0 / 59 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Watery eye			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	25 / 59 (42.37%)	1 / 26 (3.85%)	
occurrences (all)	25	1	
Diarrhea			
subjects affected / exposed	21 / 59 (35.59%)	2 / 26 (7.69%)	
occurrences (all)	21	2	
Distension			

subjects affected / exposed	2 / 59 (3.39%)	1 / 26 (3.85%)	
occurrences (all)	2	1	
Dysphagia			
subjects affected / exposed	0 / 59 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Flatulence			
subjects affected / exposed	1 / 59 (1.69%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
GI - Other			
subjects affected / exposed	2 / 59 (3.39%)	1 / 26 (3.85%)	
occurrences (all)	2	1	
Heartburn			
subjects affected / exposed	2 / 59 (3.39%)	1 / 26 (3.85%)	
occurrences (all)	2	1	
Hemorrhage, GI			
subjects affected / exposed	3 / 59 (5.08%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Hemorrhage, GU			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	31 / 59 (52.54%)	19 / 26 (73.08%)	
occurrences (all)	31	19	
Teeth			
subjects affected / exposed	0 / 59 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Ulcer, GI			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	17 / 59 (28.81%)	6 / 26 (23.08%)	
occurrences (all)	17	6	
Enteritis			
subjects affected / exposed	2 / 59 (3.39%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Fistula; GI			

subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Hemorrhoids			
subjects affected / exposed	3 / 59 (5.08%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Perforation GI			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Hepatobiliary - Other			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Inflammation/ Infection of bile duct			
subjects affected / exposed	3 / 59 (5.08%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Liver dysfunction			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	40 / 59 (67.80%)	4 / 26 (15.38%)	
occurrences (all)	40	4	
Alopecia			
subjects affected / exposed	12 / 59 (20.34%)	5 / 26 (19.23%)	
occurrences (all)	12	5	
Dry skin			
subjects affected / exposed	40 / 59 (67.80%)	0 / 26 (0.00%)	
occurrences (all)	40	0	
Hand-foot syndrome			
subjects affected / exposed	7 / 59 (11.86%)	0 / 26 (0.00%)	
occurrences (all)	7	0	
Nail changes			
subjects affected / exposed	18 / 59 (30.51%)	0 / 26 (0.00%)	
occurrences (all)	18	0	
Petechiae			

subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Photosensitivity			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	23 / 59 (38.98%)	0 / 26 (0.00%)	
occurrences (all)	23	0	
Rash			
subjects affected / exposed	34 / 59 (57.63%)	5 / 26 (19.23%)	
occurrences (all)	34	5	
Rhagades			
subjects affected / exposed	12 / 59 (20.34%)	1 / 26 (3.85%)	
occurrences (all)	12	1	
Sweating			
subjects affected / exposed	2 / 59 (3.39%)	2 / 26 (7.69%)	
occurrences (all)	2	2	
Dermatology - other			
subjects affected / exposed	5 / 59 (8.47%)	0 / 26 (0.00%)	
occurrences (all)	5	0	
Renal and urinary disorders			
Renal - Other			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Renal failure			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Urinary frequency			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 59 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Infections and infestations			

Infection			
subjects affected / exposed	24 / 59 (40.68%)	6 / 26 (23.08%)	
occurrences (all)	24	6	
Infection (Skin)			
subjects affected / exposed	2 / 59 (3.39%)	1 / 26 (3.85%)	
occurrences (all)	2	1	
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	7 / 59 (11.86%)	1 / 26 (3.85%)	
occurrences (all)	7	1	
Hypercalcemia			
subjects affected / exposed	4 / 59 (6.78%)	1 / 26 (3.85%)	
occurrences (all)	4	1	
Hyperglycemia			
subjects affected / exposed	3 / 59 (5.08%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Hyperkalemia			
subjects affected / exposed	1 / 59 (1.69%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Hypoalbuminemia			
subjects affected / exposed	1 / 59 (1.69%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Hypomagnesemia			
subjects affected / exposed	9 / 59 (15.25%)	2 / 26 (7.69%)	
occurrences (all)	9	2	
Hyponatremia			
subjects affected / exposed	2 / 59 (3.39%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Diabetes			
subjects affected / exposed	1 / 59 (1.69%)	0 / 26 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 June 2011	change of coordinating investigator
06 October 2011	changes to the central KRAS testing

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/29413685