



## 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
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##### **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/m<sup>2</sup> day 1 and day 8 / q3w

Gemcitabine 1000mg/m<sup>2</sup> 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:

<b>Subjects enrolled per age group</b>	
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
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<b>Arm title</b>	Arm A
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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/m<sup>2</sup> 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/m<sup>2</sup> 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

<b>Arm title</b>	Arm B
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Arm description:

cisplatin/gemcitabine

Arm type	Active comparator
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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/m <sup>2</sup> 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/m <sup>2</sup> day 1 and day 8 / q3w	

<b>Number of subjects in period 1</b>	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			
Cholangiocarcinoma	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
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### Dictionary used

Dictionary name	CTCAE
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Dictionary version	3.0
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### Reporting groups

Reporting group title	ArmA
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Reporting group description:

Cisplatin/Gemcitabin + Panitumumab

Reporting group title	ArmB
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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 %



<b>Non-serious adverse events</b>	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 access)			
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 occurrences (all)	8 / 59 (13.56%) 8	1 / 26 (3.85%) 1	
Dyspnea subjects affected / exposed occurrences (all)	13 / 59 (22.03%) 13	4 / 26 (15.38%) 4	
Hemorrhage pulmonary subjects affected / exposed occurrences (all)	3 / 59 (5.08%) 3	0 / 26 (0.00%) 0	
Pulmonary - Other subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 0	1 / 26 (3.85%) 1	
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	6 / 59 (10.17%) 6	1 / 26 (3.85%) 1	
Mood alteration subjects affected / exposed occurrences (all)	4 / 59 (6.78%) 4	3 / 26 (11.54%) 3	
Psychosis subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	0 / 26 (0.00%) 0	
Investigations ALT subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 0	1 / 26 (3.85%) 1	
Alkaline phosphatase subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	0 / 26 (0.00%) 0	
Bilirubin subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	0 / 26 (0.00%) 0	
Creatinine subjects affected / exposed occurrences (all)	2 / 59 (3.39%) 2	4 / 26 (15.38%) 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 occurrences (all)	5 / 59 (8.47%) 5	4 / 26 (15.38%) 4	
Tremor subjects affected / exposed occurrences (all)	3 / 59 (5.08%) 3	0 / 26 (0.00%) 0	
Blood and lymphatic system disorders Blood – Other (Specify) subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	0 / 26 (0.00%) 0	
Febrile neutropenia subjects affected / exposed occurrences (all)	4 / 59 (6.78%) 4	0 / 26 (0.00%) 0	
Hemolysis subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	0 / 26 (0.00%) 0	
Leukocytes subjects affected / exposed occurrences (all)	43 / 59 (72.88%) 43	26 / 26 (100.00%) 26	
Lymphopenia subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 0	1 / 26 (3.85%) 1	
Platelets subjects affected / exposed occurrences (all)	42 / 59 (71.19%) 42	20 / 26 (76.92%) 20	
Thrombotic microangiopathy subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 0	1 / 26 (3.85%) 1	
Hypokalaemia subjects affected / exposed occurrences (all)	3 / 59 (5.08%) 3	0 / 26 (0.00%) 0	
Ear and labyrinth disorders Auditory/Ear - Other (Specify) subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	0 / 26 (0.00%) 0	
Hearing			

subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 0	3 / 26 (11.54%) 3	
Tinnitus subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 0	2 / 26 (7.69%) 2	
Eye disorders			
Dry eye subjects affected / exposed occurrences (all)	2 / 59 (3.39%) 2	0 / 26 (0.00%) 0	
Eyelid dysfunction subjects affected / exposed occurrences (all)	2 / 59 (3.39%) 2	0 / 26 (0.00%) 0	
Flashing lights subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 0	2 / 26 (7.69%) 2	
Ocular - Other subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 0	2 / 26 (7.69%) 2	
Ocular surface disease subjects affected / exposed occurrences (all)	5 / 59 (8.47%) 5	0 / 26 (0.00%) 0	
Vitreous hemorrhage subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 0	1 / 26 (3.85%) 1	
Watery eye subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	0 / 26 (0.00%) 0	
Gastrointestinal disorders			
Constipation subjects affected / exposed occurrences (all)	25 / 59 (42.37%) 25	1 / 26 (3.85%) 1	
Diarrhea subjects affected / exposed occurrences (all)	21 / 59 (35.59%) 21	2 / 26 (7.69%) 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 occurrences (all)	1 / 59 (1.69%) 1	0 / 26 (0.00%) 0	
Hemorrhoids subjects affected / exposed occurrences (all)	3 / 59 (5.08%) 3	0 / 26 (0.00%) 0	
Perforation GI subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	0 / 26 (0.00%) 0	
Hepatobiliary disorders Hepatobiliary - Other subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	0 / 26 (0.00%) 0	
Inflammation/ Infection of bile duct subjects affected / exposed occurrences (all)	3 / 59 (5.08%) 3	0 / 26 (0.00%) 0	
Liver dysfunction subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	0 / 26 (0.00%) 0	
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all)	40 / 59 (67.80%) 40	4 / 26 (15.38%) 4	
Alopecia subjects affected / exposed occurrences (all)	12 / 59 (20.34%) 12	5 / 26 (19.23%) 5	
Dry skin subjects affected / exposed occurrences (all)	40 / 59 (67.80%) 40	0 / 26 (0.00%) 0	
Hand-foot syndrome subjects affected / exposed occurrences (all)	7 / 59 (11.86%) 7	0 / 26 (0.00%) 0	
Nail changes subjects affected / exposed occurrences (all)	18 / 59 (30.51%) 18	0 / 26 (0.00%) 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:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

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