Clinical trial results:
Perioperative chemotherapy with FOLFOX plus Cetuximab versus adjuvant FOLFOX plus Cetuximab for patients with resectable liver metastases of colorectal carcinoma

Summary

EudraCT number	2008-005312-41
Trial protocol	DE AT
Global end of trial date	31 March 2015

Results information

Result version number	v1 (current)
This version publication date	26 May 2016
First version publication date	26 May 2016
Summary attachment (see zip file)	ClinicalTrialReport2008-005312-41 (Panter-csr-v0.1-20160122-2016-04-13_signed.pdf)

Trial information

Trial identification

Sponsor protocol code	Panter_2008

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01266187
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	RWTH Aachen University, Mrs Dipl. Biol. Verena Deserno
Sponsor organisation address	Pauwelsstraße 30, Aachen, Germany, 52074
Public contact	Verena Deserno, RWTH Aachen University, Clinical Trials Center Aachen (CTC-A),, 49 2418035849, vdeserno@ukaachen.de
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	22 January 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 March 2015
Global end of trial reached?	Yes
Global end of trial date	31 March 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The first primary objective of the study is to compare the postoperative complication rate according to Clavien score (> grade 1) of a perioperative chemotherapy with a postoperative regimen.
A second primary objective of the study is to compare for the patient subgroup with >3 liver metastases or at least one metastasis ≥ 5 cm in diameter the median disease free survival.

Protection of trial subjects:

The included cancer patients were treated with morphine derivatives as pain relievers if necessary.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 24
Worldwide total number of subjects	24
EEA total number of subjects	24

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)	10

From 65 to 84 years	14
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients will be recruited in large centres. Patients with resectable colorectal liver metastases who are willing to
participate will enter the screening phase. Prior to the start, subjects will perform the screening period in order to
check if all eligibility criteria are fulfilled. Eligible patients will be randomized wihtin 3 weeks.

Pre-assignment

Screening details:

Inclusion criteria: signed written informed consent; ≥ 18 years; Proven K-RAS wildtype in primary tumour or metastasis tissue; Diagnosis of resectable metachronous liver-metastases after complete resection (R0) of primary tumour without gross or microscopic evidence of residual disease

Period 1

Period 1 title	FOLFOX plus Cetuximab (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

12 postoperative cycles of Cetuximab and FOLFOX

Arm type	Experimental
Investigational medicinal product name	Cetuximab
Investigational medicinal product code	
Other name	ERBITUX
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

initial dose 400 mg/m2 and subsequent weekly doses of 250 mg/m2

Investigational medicinal product name	Folinic acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

400 mg/m²

Investigational medicinal product name	5-Fluorouracil (5-FU)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous use, Intravenous bolus use

Dosage and administration details:

400 mg/m² i.v. bolus followed by 2400 - 3000 mg/m² continuous infusion

Investigational medicinal product name	Oxaliplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous use

Dosage and administration details: 85 mg/m² infusion (2 h)

Arm title	Arm B
Arm description: 6 cycles before sugery and 6 cycles after the surgery	
Arm type	Experimental
Investigational medicinal product name	Cetuximab
Investigational medicinal product code	
Other name	ERBITUX
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous use
Dosage and administration details: initial dose 400 mg/m2 and subsequent weekly doses of 250 mg/m2	
Investigational medicinal product name	Folinic acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous use
Dosage and administration details: 400 mg/m²	
Investigational medicinal product name	5-Fluorouracil (5-FU)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous bolus use , Intravenous use
Dosage and administration details: 400 mg/m² i.v. bolus followed by 2400 - 3000 mg/m² continuous infusion	
Investigational medicinal product name	Oxaliplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous use
Dosage and administration details: 85 mg/m² infusion (2 h)	

Number of subjects in period 1	Arm A	Arm B
Started	11	13
Completed	11	13

Baseline characteristics

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description:	
12 postoperative cycles of Cetuximab and FOLFOX	
Reporting group title	Arm B
Reporting group description:	
6 cycles before sugery and 6 cycles after the surgery	
Subject analysis set title	ITT Analysis
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Since the study was stopped prematurely, all analyses were done for the ITT-set, except the safety analyses, which were done for the safety population and the primary endpoint analysis, which was done for the surgery population. Results will be presented overall and according to the following treatment arms Arm A: Surgery 4-8 weeks rest 24 weeks FOLFOX + Cetuximab Arm B: 12 weeks FOLFOX + Cetuximab 4 weeks rest surgery 4-8 weeks rest 12 weeks FOLFOX + Cetuximab	

Primary: The primary endpoint is the post-operative complication rate (Clavien score > grade 1) up to the 30th postoperative day or the day of discharge from hospital

End point title	The primary endpoint is the post-operative complication rate (Clavien score > grade 1) up to the 30th postoperative day or the day of discharge from hospital
End point description:	
12.3.1 Hypotheses for the First Primary Endpoint The null hypothesis is that the postoperative complication rate (≥ grade I according Dindo et.al.) is equal between the arm treated with perioperative therapy and the arm treated with adjuvant therapy. The alternative hypothesis is that the postoperative complication rate differs between these two arms.	
End point type	Primary
End point timeframe:	
up to the 30th postoperative day or the day of discharge from hospital.	

End point values	Arm A	Arm B	ITT Analysis	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	11	13	24	
Units: Clavien score > grade 1	11	13	24	

Statistical analyses

Statistical analysis title	two sided Cochran-Mantel-Haenszel (CMH) test
Statistical analysis description:	
Postoperative complications grade > 1 in both treatment arms were compared using the two sided Cochran-Mantel-Haenszel (CMH) test stratified for Fong Score, tumour volume and Study Site at a two-sided significance level of 0.05. The primary analysis for the post-operative complication rate was performed in all patients with surgery for liver resection. An intention-to-treat	

analysis was also planned in all randomized patients.

Comparison groups	Arm A v Arm B v ITT Analysis
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence[1]
P-value	< 0.05
Method	Cochran-Mantel-Haenszel
Parameter estimate	Cox proportional hazard
Point estimate	0.14208
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.078
upper limit	17.008
Variability estimate	Standard error of the mean

Notes:

[1] - The following two null hypotheses will be tested confirmatory in hierarchical order, so that no alpha adjustment is necessary.
The null hypothesis is that the postoperative complication rate (≥ grade I according Dindo et.al.) is equal between the arm treated with perioperative therapy and the arm treated with adjuvant therapy.
The alternative hypothesis is that the postoperative complication rate differs between these two arms.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs will be entered in the case report form. Sponsor must be informed within 24 h of SAEs/ significant side effects/ deaths.

Adverse event reporting additional description:

The Investigator will collect adverse events by asking the subject a general question ("how did you feel since last visit"). Also, the Investigator will ask the subject whether (s)he has experienced any symptoms or discomfort since the last visit (non-leading question).

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13

Reporting groups

Reporting group title	Arm A

Reporting group description:

A total of 314 adverse events (AEs) occurred in 19 patients, who received chemotherapy in both arms (Listing 14, section 13.2.6). 90 AEs occurred in Arm A and 224 in Arm B. 6 of the 19 patients showed SAEs, 4 in Arm A and 2 in Arm B (Table 16).

Reporting group title	Arm B

Reporting group description:

A total of 314 adverse events (AEs) occurred in 19 patients, who received chemotherapy in both arms (Listing 14, section 13.2.6). 90 AEs occurred in Arm A and 224 in Arm B. 6 of the 19 patients showed SAEs, 4 in Arm A and 2 in Arm B (Table 16).

Serious adverse events	Arm A	Arm B	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 11 (36.36%)	2 / 13 (15.38%)	
number of deaths (all causes)	1	2	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Jugular vein thrombosis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (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			
Pyrexia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	2 / 11 (18.18%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorder			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	2 / 11 (18.18%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Arm A	Arm B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 11 (63.64%)	12 / 13 (92.31%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified (incl cysts and polyps) - Other			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Vascular disorders - Other			
subjects affected / exposed	1 / 11 (9.09%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Visceral arterial ischemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Edema trunk			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	0 / 11 (0.00%)	3 / 13 (23.08%)	
occurrences (all)	0	3	
Fever			
subjects affected / exposed	3 / 11 (27.27%)	1 / 13 (7.69%)	
occurrences (all)	3	1	
General disorders and administration site conditions - Other			

subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Hematoma			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Infusion related reaction			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Pain			
subjects affected / exposed	2 / 11 (18.18%)	2 / 13 (15.38%)	
occurrences (all)	2	2	
Palmar-plantar erythrodysesthesia syndrome			
subjects affected / exposed	1 / 11 (9.09%)	2 / 13 (15.38%)	
occurrences (all)	1	2	
Immune system disorders			
Allergic reaction			
subjects affected / exposed	2 / 11 (18.18%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	1 / 11 (9.09%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Hoarseness			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Hypoxia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Pleural effusion			
subjects affected / exposed	2 / 11 (18.18%)	1 / 13 (7.69%)	
occurrences (all)	2	1	
Pneumothorax			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Productive cough			

subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Psychiatric disorders			
Aphonia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Delirium			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Hallucinations			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Investigations			
Investigations - Other			
subjects affected / exposed	0 / 11 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Injury, poisoning and procedural complications			
Seroma			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Cardiac disorders			
Cardiac disorders - Other			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Chest pain - cardiac			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	0 / 11 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Hypotension			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences (all)	1	0	

Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Dysgeusia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Nervous system disorders			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Paresthesia			
subjects affected / exposed	2 / 11 (18.18%)	2 / 13 (15.38%)	
occurrences (all)	2	2	
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 11 (9.09%)	4 / 13 (30.77%)	
occurrences (all)	1	4	
Vertigo			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	2 / 11 (18.18%)	1 / 13 (7.69%)	
occurrences (all)	2	1	
Anorexia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders - Other			
subjects affected / exposed	2 / 11 (18.18%)	2 / 13 (15.38%)	
occurrences (all)	2	2	
Febrile neutropenia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Leukocytosis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Neutrophil count decreased			

subjects affected / exposed	1 / 11 (9.09%)	3 / 13 (23.08%)	
occurrences (all)	1	3	
Platelet count decreased			
subjects affected / exposed	3 / 11 (27.27%)	3 / 13 (23.08%)	
occurrences (all)	3	3	
Thromboembolic event			
subjects affected / exposed	3 / 11 (27.27%)	1 / 13 (7.69%)	
occurrences (all)	3	1	
White blood cell decreased			
subjects affected / exposed	0 / 11 (0.00%)	3 / 13 (23.08%)	
occurrences (all)	0	3	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 11 (18.18%)	3 / 13 (23.08%)	
occurrences (all)	2	3	
Constipation			
subjects affected / exposed	1 / 11 (9.09%)	3 / 13 (23.08%)	
occurrences (all)	1	3	
Dehydration			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Diarrhea			
subjects affected / exposed	4 / 11 (36.36%)	5 / 13 (38.46%)	
occurrences (all)	4	5	
Gastrointestinal disorders - Other			
subjects affected / exposed	3 / 11 (27.27%)	0 / 13 (0.00%)	
occurrences (all)	3	0	
Nausea			
subjects affected / exposed	3 / 11 (27.27%)	6 / 13 (46.15%)	
occurrences (all)	3	6	
Rectal obstruction			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	1 / 11 (9.09%)	1 / 13 (7.69%)	
occurrences (all)	1	1	

Hepatobiliary disorders			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Biliary anastomotic leak			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Blood bilirubin increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
GGT increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Hepatic hemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Hepatobiliary disorders - Other			
subjects affected / exposed	1 / 11 (9.09%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 11 (0.00%)	3 / 13 (23.08%)	
occurrences (all)	0	3	
Bruising			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Dry skin			
subjects affected / exposed	0 / 11 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Papulopustular rash			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Pruritus			

subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Rash acneiform			
subjects affected / exposed	4 / 11 (36.36%)	9 / 13 (69.23%)	
occurrences (all)	4	9	
Rash maculo-papular			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders - Other			
subjects affected / exposed	1 / 11 (9.09%)	4 / 13 (30.77%)	
occurrences (all)	1	4	
Thrombotic thrombocytopenic purpura			
subjects affected / exposed	2 / 11 (18.18%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Renal and urinary disorders			
Prostatic obstruction			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Bone marrow hypocellular			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Gynecomastia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Infections and infestations			
Abdominal infection			
subjects affected / exposed	1 / 11 (9.09%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Breast infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	

Bronchial infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Conjunctivitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Gum infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Infections and infestations - Other			
subjects affected / exposed	1 / 11 (9.09%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Lung infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Mucositis oral			
subjects affected / exposed	3 / 11 (27.27%)	5 / 13 (38.46%)	
occurrences (all)	3	5	
Wound infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Hyperglycemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Hyperkalemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Hypocalcemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Hypokalemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 January 2015	10.3 Definition of the end of study According to the Amendment No. 1, the end of study is defined as the date of the approval of the German or Austrian Competent Authority or the positive opinion of the German or Austrian Ethics Committee for the Amendment No. 1, whatever is dated the latest

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported