Clinical trial results:
Phase II, Exploratory, Multicenter, Non Randomized, Single Agent Cohort Study to Determine Best Tumor Response With Trastuzumab Emtansine in HER2 Overexpressing Solid Tumors

Summary

EudraCT number	2015-001377-40
Trial protocol	ES SK NL IT
Global end of trial date	10 April 2018

Results information

Result version number	v1 (current)
This version publication date	25 April 2019
First version publication date	25 April 2019

Trial information

Trial identification

Sponsor protocol code	MO29694

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02999672
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Medical Communications, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
Scientific contact	Medical Communications, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 April 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 April 2018
Global end of trial reached?	Yes
Global end of trial date	10 April 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy and safety of trastuzumab emtansine.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 October 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	18 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Spain: 9
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	12
From 65 to 84 years	8

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

315 patients were screened.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1 (UBC)

Arm description:

First six participants with locally advanced (unresectable and not treatable with curative intent) or metastatic UBC initially received Regimen A (trastuzumab emtansine at a dose of 2.4 mg/kg qw). An iDMC assessed the safety among the first six participants and decided whether dose would be switched to Regimen B (trastuzumab emtansine at a dose of 3.6 mg/kg q3w).

Arm type	Experimental
Investigational medicinal product name	Trastuzumab Emtansine
Investigational medicinal product code	
Other name	Kadcyla
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Trastuzumab emtansine will be administered as Regimen A (2.4 mg/kg qw via IV infusion) or Regimen B (3.6 mg/kg q3w via IV infusion) until unacceptable toxicity, withdrawal of consent, disease progression, or death, whichever occurs first.

Arm title	Cohort 2 (Pancreatic cancer/cholangiocarcinoma)

Arm description:

First six participants with metastatic pancreatic cancer/cholangiocarcinoma received Regimen A (trastuzumab emtansine at a dose of 2.4 mg/kg qw). An iDMC assessed the safety among the first six participants and decided whether dose would be switched to Regimen B (trastuzumab emtansine at a dose of 3.6 mg/kg q3w).

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Investigational medicinal product name	Trastuzumab Emtansine
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Number of subjects in period 1	Cohort 1 (UBC)	Cohort 2 (Pancreatic cancer/cholangiocarcinoma)
Started	13	7
Completed	0	0
Not completed	13	7
Adverse event, non-fatal	4	-
Progressive Disease	9	6
Study Terminated by Sponsor	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1 (UBC)
Reporting group description:	
First six participants with locally advanced (unresectable and not treatable with curative intent) or metastatic UBC initially received Regimen A (trastuzumab emtansine at a dose of 2.4 mg/kg qw). An iDMC assessed the safety among the first six participants and decided whether dose would be switched to Regimen B (trastuzumab emtansine at a dose of 3.6 mg/kg q3w).	
Reporting group title	Cohort 2 (Pancreatic cancer/cholangiocarcinoma)
Reporting group description:	
First six participants with metastatic pancreatic cancer/cholangiocarcinoma received Regimen A (trastuzumab emtansine at a dose of 2.4 mg/kg qw). An iDMC assessed the safety among the first six participants and decided whether dose would be switched to Regimen B (trastuzumab emtansine at a dose of 3.6 mg/kg q3w).	

Reporting group values	Cohort 1 (UBC)	Cohort 2 (Pancreatic cancer/cholangiocarcinoma)	Total
Number of subjects	13	7	20
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	7	5	12
From 65-84 years	6	2	8
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	57.5	62.9	
standard deviation	± 14.1	± 7.2	-
Sex: Female, Male Units: Subjects			
Female	1	3	4
Male	12	4	16
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	0	2
Not Hispanic or Latino	9	7	16
Unknown or Not Reported	2	0	2
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0

Black or African American	0	0	0
White	12	7	19
More than one race	0	0	0
Unknown or Not Reported	1	0	1

End points

End points reporting groups

Reporting group title	Cohort 1 (UBC)

Reporting group description:

First six participants with locally advanced (unresectable and not treatable with curative intent) or metastatic UBC initially received Regimen A (trastuzumab emtansine at a dose of 2.4 mg/kg qw). An iDMC assessed the safety among the first six participants and decided whether dose would be switched to Regimen B (trastuzumab emtansine at a dose of 3.6 mg/kg q3w).

Reporting group title	Cohort 2 (Pancreatic cancer/cholangiocarcinoma)

Reporting group description:

First six participants with metastatic pancreatic cancer/cholangiocarcinoma received Regimen A (trastuzumab emtansine at a dose of 2.4 mg/kg qw). An iDMC assessed the safety among the first six participants and decided whether dose would be switched to Regimen B (trastuzumab emtansine at a dose of 3.6 mg/kg q3w).

Primary: Best Overall Response (BOR) assessed by the investigator using Response Evaluation Criteria in Solid Tumors [RECIST] 1.1).

End point title	Best Overall Response (BOR) assessed by the investigator using Response Evaluation Criteria in Solid Tumors [RECIST] 1.1).[1]

End point description:

BOR is defined as the best response recorded from the first day of study treatment until disease progression/recurrence or death. Responders, as assessed every 6 weeks, were defined based on tumor assessment status as partial responder (PR) or complete responder (CR) at these time points. To be assigned a status of PR or CR (i.e.,a responder), changes in tumor measurements had to be confirmed by repeat assessments that should be performed no less than 4 weeks after the criteria for response were first met, i.e., patients needed to have 2 consecutive assessments of PR or CR to be a responder.

End point type	Primary

End point timeframe:

Baseline up to PD/recurrence or death, whichever occurs first (up to approximately 18 months)

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: Due to early termination of the study, all statistical analyses were based only on descriptive statistics, including confidence intervals as relevant.

End point values	Cohort 1 (UBC)	Cohort 2 (Pancreatic cancer/cholangiocarcinoma)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	7		
Units: Percentage of Treated Participants				
number (not applicable)				
CR	0	0		
PR	38.5	14.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS)

End point description:

PFS was defined as the time from beginning of treatment to the first occurrence of disease progression, as determined by the investigator (uding RECIST 1.1), or death from any cause, whichever occurs first.

End point type	Secondary

End point timeframe:

Baseline up to PD/recurrence or death, whichever occurs first (up to approximately 18 months)

End point values	Cohort 1 (UBC)	Cohort 2 (Pancreatic cancer/cholangiocarcinoma)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	7		
Units: Months				
median (confidence interval 95%)	2.20 (1.18 to 4.30)	2.58 (1.31 to 9.99)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS was determined as the time from beginning of treatment to death from any cause. A value of "99999" represents a non-estimable number, as the study was terminated before a sufficient amount of data could be collected for accurate calculation.

End point type	Secondary

End point timeframe:

Baseline up to PD/recurrence or death, whichever occurs first (up to approximately 18 months)

End point values	Cohort 1 (UBC)	Cohort 2 (Pancreatic cancer/cholangiocarcinoma)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	7		
Units: Months				
median (confidence interval 95%)	7.03 (3.75 to 99999)	99999 (1.45 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Adverse Events (AEs) and Serious AEs (SAEs)

End point title	Percentage of Participants With Adverse Events (AEs) and Serious AEs (SAEs)

End point description:

Incidence, type and severity of all adverse events (AEs) and serious adverse events (SAEs), based on National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE v4.03).

End point type	Secondary

End point timeframe:

Baseline up to approximately 18 months

End point values	Cohort 1 (UBC)	Cohort 2 (Pancreatic cancer/cholangiocarcinoma)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	7		
Units: Percentage of Participants				
number (not applicable)				
AEs	84.6	100		
Grade 1 AE	7.7	14.3		
Grade 2 AE	23.1	57.1		
Grade 3 AE	30.8	28.1		
Grade 4 AE	0	0		
Grade 5 AE	23.1	0		
AE greater than Grade 3	53.8	28.6		
AE related to Trastuzumab Emtansine (TE)	84.6	85.7		
SAEs	46.2	28.6		
SAE related to TE	0	0		
AE with fatal outcome	23.1	0		
AE leading to discontinuation of TE	23.1	0		
AE leading to modification of TE	61.5	57.1		
AE of special interest	0	0		
SAE of special interest	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Drug-induced Liver Injury Meeting Hy's Law Criteria

End point title	Percentage of Participants With Drug-induced Liver Injury Meeting Hy's Law Criteria

End point description:

Participants from both cohorts (UBC and Pancreatic cancer/cholangiocarcinoma) were analyzed for drug-induced liver injury following Hy's Law. Hy's Law criteria for potential drug-induced liver injury includes an elevated ALT (alanine aminotransferase) or AST (aspartate aminotransferase) in combination with either elevated bilirubin or clinical jaundice.

End point type	Secondary

End point timeframe:

Baseline up to approximately 18 months

End point values	Cohort 1 (UBC)	Cohort 2 (Pancreatic cancer/cholangiocarcinoma)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	7		
Units: Percentage of Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma/Serum Concentrations of Trastuzumab Emtansine

End point title	Plasma/Serum Concentrations of Trastuzumab Emtansine

End point description:

Samples for evaluation of trastuzumab emtansine, DM1, and total trastuzumab were obtained from all participants from both cohorts at specified time points. A value of "99999" represents a non-estimable number, as the study was terminated before a sufficient amount of data could be collected for accurate calculation.

End point type	Secondary

End point timeframe:

Regimen A: predose (0 minutes [min]) and 15-30 min postinfusion on Days (D) 1, 8, 15 of Cycle (C) 1 and D1C4; predose on D1C2. Regimen B: predose and 15-30 min postinfusion on D1C1 and D1C4; predose on D1C2. 1 Cycle=21 days

End point values	Cohort 1 (UBC)	Cohort 2 (Pancreatic cancer/cholangiocarcinoma)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	7		
Units: ng/mL				

arithmetic mean (standard deviation)				
Predose, D1C1	99999 (± 99999)	99999 (± 99999)		
15-30 min post-infusion, D1C1	99999 (± 99999)	99999 (± 99999)		
Predose, D8C1	99999 (± 99999)	99999 (± 99999)		
15-30 min post-infusion, D1C8	99999 (± 99999)	99999 (± 99999)		
Predose, D15C1	99999 (± 99999)	99999 (± 99999)		
15-30 min post-infusion, D15C8	99999 (± 99999)	99999 (± 99999)		
Predose, D1C2	99999 (± 99999)	99999 (± 99999)		
Predose, D1C4	99999 (± 99999)	99999 (± 99999)		
15-30 min post-infusion, D1C4	99999 (± 99999)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to approximately 18 months

Adverse event reporting additional description:

An Adverse Event (AE) is any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medical treatment or procedure that may or may not be considered related to the medical treatment or procedure.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Cohort 1 (UBC)

Reporting group description:

First six participants with locally advanced (unresectable and not treatable with curative intent) or metastatic UBC initially received Regimen A (trastuzumab emtansine at a dose of 2.4 mg/kg qw). An iDMC assessed the safety among the first six participants and decided whether dose would be switched to Regimen B (trastuzumab emtansine at a dose of 3.6 mg/kg q3w).

Reporting group title	Cohort 2 (Pancreatic cancer/cholangiocarcinoma)

Reporting group description:

First six participants with metastatic pancreatic cancer/cholangiocarcinoma received Regimen A (trastuzumab emtansine at a dose of 2.4 mg/kg qw). An iDMC assessed the safety among the first six participants and decided whether dose would be switched to Regimen B (trastuzumab emtansine at a dose of 3.6 mg/kg q3w).

Serious adverse events	Cohort 1 (UBC)	Cohort 2 (Pancreatic cancer/cholangiocarcinoma)	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 13 (46.15%)	2 / 7 (28.57%)	
number of deaths (all causes)	7	1	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Craniocerebral injury			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pulmonary sepsis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	2 / 13 (15.38%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device-related sepsis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cohort 1 (UBC)	Cohort 2 (Pancreatic cancer/cholangiocarcinoma)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 13 (84.62%)	7 / 7 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 13 (30.77%)	2 / 7 (28.57%)	
occurrences (all)	5	5	
Influenza like Illness			
subjects affected / exposed	2 / 13 (15.38%)	1 / 7 (14.29%)	
occurrences (all)	2	1	
Oedema peripheral			
subjects affected / exposed	1 / 13 (7.69%)	1 / 7 (14.29%)	
occurrences (all)	1	2	
Pyrexia			
subjects affected / exposed	5 / 13 (38.46%)	3 / 7 (42.86%)	
occurrences (all)	6	6	
Chills			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Fatigue			

subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	
Malaise			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 13 (7.69%)	2 / 7 (28.57%)	
occurrences (all)	1	4	
Dyspnoea			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Epistaxis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Dysphonia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Psychiatric disorders			
Restlessness			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Affective disorder			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Depression			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Insomnia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 13 (15.38%)	1 / 7 (14.29%)	
occurrences (all)	2	1	
Aspartate aminotransferase increased			

subjects affected / exposed	3 / 13 (23.08%)	1 / 7 (14.29%)	
occurrences (all)	3	1	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 13 (7.69%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Blood phosphorus decreased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Neutrophil count decreased			
subjects affected / exposed	1 / 13 (7.69%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Platelet count decreased			
subjects affected / exposed	2 / 13 (15.38%)	2 / 7 (28.57%)	
occurrences (all)	2	3	
Transaminases increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Blood bilirubin increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Lymphocyte count decreased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Weight decreased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
White blood cell count decreased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			

Fall			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Infusion related reaction			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Ventricular dysfunction			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	1 / 13 (7.69%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Meralgia paraesthetica			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 13 (7.69%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Dysgeusia			
subjects affected / exposed	0 / 13 (0.00%)	2 / 7 (28.57%)	
occurrences (all)	0	3	
Paraesthesia			
subjects affected / exposed	0 / 13 (0.00%)	3 / 7 (42.86%)	
occurrences (all)	0	5	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 13 (23.08%)	1 / 7 (14.29%)	
occurrences (all)	3	1	
Lymphopenia			
subjects affected / exposed	1 / 13 (7.69%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Thrombocytopenia			

subjects affected / exposed	3 / 13 (23.08%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Leukocytosis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Neutropenia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Neutrophilia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Eye disorders			
Lacrimation increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Photophobia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	2 / 13 (15.38%)	1 / 7 (14.29%)	
occurrences (all)	2	1	
Diarrhoea			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Dry mouth			
subjects affected / exposed	1 / 13 (7.69%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Intestinal obstruction			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Vomiting			

subjects affected / exposed	2 / 13 (15.38%)	1 / 7 (14.29%)	
occurrences (all)	2	1	
Abdominal discomfort			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Abdominal pain			
subjects affected / exposed	0 / 13 (0.00%)	4 / 7 (57.14%)	
occurrences (all)	0	5	
Abdominal pain, upper			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Dyspepsia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Gastric ulcer			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	0 / 13 (0.00%)	3 / 7 (42.86%)	
occurrences (all)	0	4	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Dermatitis acneiform			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Cystitis noninfective			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Haematuria			
subjects affected / exposed	3 / 13 (23.08%)	0 / 7 (0.00%)	
occurrences (all)	4	0	
Pollakiuria			

subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Renal failure			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 13 (15.38%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Back pain			
subjects affected / exposed	1 / 13 (7.69%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Bone pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Neck pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	1 / 13 (7.69%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 13 (7.69%)	3 / 7 (42.86%)	
occurrences (all)	1	4	
Diabetes mellitus			
subjects affected / exposed	0 / 13 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Hypoalbuminaemia			

subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 7 (14.29%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 February 2017	Changes to outcome measures and eligibility criteria

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The results represent the data up to primary completion date (10 April 2018). However, due to the early termination, the study was unable to fully address its primary and secondary objectives.

Notes: