Clinical trial results:
Phase II Trial of CAP7.1 in adult patients with refractory malignancies Small cell lung carcinoma, Non-small cell lung carcinoma, Biliary carcinoma

Summary

EudraCT number	2012-002378-30
Trial protocol	DE
Global end of trial date	10 April 2017

Results information

Result version number	v1 (current)
This version publication date	29 August 2018
First version publication date	29 August 2018

Trial information

Trial identification

Sponsor protocol code	CPN710102

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02094560
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CellAct Pharma GmbH
Sponsor organisation address	Biomedizin Zentrum Dortmund, Otto-Hahn-Str. 15, Dortmund, Germany, 44227
Public contact	Nalân Utku, CellAct Pharma GmbH, 49 23197426350, n.utku@cellact.eu
Scientific contact	Nalân Utku, CellAct Pharma GmbH, 49 23197426350, n.utku@cellact.eu
Sponsor organisation name	Mundipharma EDO GmbH
Sponsor organisation address	St. Alban-Rheinweg 74, Basel, Switzerland, CH-4020
Public contact	Thomas Mehrling, Mundiparma EDO GmbH, 41 61 205 1473, thomas.mehrling@edoncology.com
Scientific contact	Thomas Mehrling, Mundiparma EDO GmbH, 41 61 205 1473, thomas.mehrling@edoncology.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	02 December 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 April 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was to assess the antitumor activity of CAP7.1 based on the observed objective response rate and rate of disease stabilization using Response Evaluation Criteria in Solid Tumours (RECIST) 1.1.

Protection of trial subjects:

The study was conducted in agreement with the Declaration of Helsinki (Tokyo, Venice, Hong Kong, Somerset West and Edinburgh amendments) and the laws and regulations of the country, whichever provides the greatest protection of the subject.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 November 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 43
Worldwide total number of subjects	43
EEA total number of subjects	43

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)	22

From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Overall 45 subjects were enrolled, Of them 43 subjects were treated.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Non-Small Cell Lung Cancer (NSCLC): CAP7.1

Arm description:

Subjects with NSCLC who had progressed despite previous therapies received 60 minutes (min) intravenous infusion of 150 or 200 milligram per square meter (mg/m^2) CAP7.1 daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

Arm type	Experimental
Investigational medicinal product name	CAP7.1
Investigational medicinal product code	CAP7.1
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received 150 or 200 mg/m^2 (60 min intravenous infusion) of CAP7.1.

Arm title	Non-Small Cell Lung Cancer (NSCLC): Best Supportive Care (BSC)

Arm description:

Subjects with NSCLC who had progressed despite previous therapies received best support as per institutional standards. In case of progression, these subjects were allowed to cross over to CAP7.1 therapy at the dose of 150 or 200 mg/m^2 (60 min intravenous infusion) daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

Arm type	Best Supportive Care

No investigational medicinal product assigned in this arm

Arm title	Small Cell Lung Cancer (SCLC): CAP7.1

Arm description:

Subjects with SCLC who had progressed despite previous therapies received 60 min intravenous infusion of 150 or 200 mg/m^2 CAP7.1 daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

Arm type	Experimental

Investigational medicinal product name	CAP7.1
Investigational medicinal product code	CAP7.1
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received 150 or 200 mg/m^2 (60 min intravenous infusion) of CAP7.1.

Arm title	Biliary tract cancer: CAP7.1

Arm description:

Subjects with advanced biliary tract cancer who had progressed despite previous therapies received 60 min intravenous infusion of 150 or 200 mg/m^2 CAP7.1 daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

Arm type	Experimental
Investigational medicinal product name	CAP7.1
Investigational medicinal product code	CAP7.1
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received 150 or 200 mg/m^2 (60 min intravenous infusion) of CAP7.1.

Arm title	Biliary tract cancer: Best Supportive Care (BSC)

Arm description:

Subjects with advanced biliary tract cancer who had progressed despite previous therapies received best support as per institutional standards. In case of progression, these subjects were allowed to cross over to CAP7.1 therapy at the dose of 150 or 200 mg/m^2 (60 min intravenous infusion) daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

Arm type	Best Supportive Care

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Non-Small Cell Lung Cancer (NSCLC): CAP7.1	Non-Small Cell Lung Cancer (NSCLC): Best Supportive Care (BSC)	Small Cell Lung Cancer (SCLC): CAP7.1
Started	4	4	8
Completed	2	0	4
Not completed	2	4	4
Consent withdrawn by subject	-	2	-
Physician decision	-	-	-
Removed Medically Warranted	-	1	-
Other	-	-	-
Progressive Disease	1	1	3
Screening Failure	-	-	-
Adverse event	1	-	1

Lost to follow-up	-	-	-

Number of subjects in period 1	Biliary tract cancer: CAP7.1	Biliary tract cancer: Best Supportive Care (BSC)
Started	14	13
Completed	9	5
Not completed	5	8
Consent withdrawn by subject	-	1
Physician decision	-	1
Removed Medically Warranted	-	-
Other	1	1
Progressive Disease	-	1
Screening Failure	1	-
Adverse event	3	3
Lost to follow-up	-	1

Baseline characteristics

Reporting groups

Reporting group title	Non-Small Cell Lung Cancer (NSCLC): CAP7.1

Reporting group description:

Subjects with NSCLC who had progressed despite previous therapies received 60 minutes (min) intravenous infusion of 150 or 200 milligram per square meter (mg/m^2) CAP7.1 daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

Reporting group title	Non-Small Cell Lung Cancer (NSCLC): Best Supportive Care (BSC)

Reporting group description:

Subjects with NSCLC who had progressed despite previous therapies received best support as per institutional standards. In case of progression, these subjects were allowed to cross over to CAP7.1 therapy at the dose of 150 or 200 mg/m^2 (60 min intravenous infusion) daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

Reporting group title	Small Cell Lung Cancer (SCLC): CAP7.1

Reporting group description:

Subjects with SCLC who had progressed despite previous therapies received 60 min intravenous infusion of 150 or 200 mg/m^2 CAP7.1 daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

Reporting group title	Biliary tract cancer: CAP7.1

Reporting group description:

Subjects with advanced biliary tract cancer who had progressed despite previous therapies received 60 min intravenous infusion of 150 or 200 mg/m^2 CAP7.1 daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

Reporting group title	Biliary tract cancer: Best Supportive Care (BSC)

Reporting group description:

Subjects with advanced biliary tract cancer who had progressed despite previous therapies received best support as per institutional standards. In case of progression, these subjects were allowed to cross over to CAP7.1 therapy at the dose of 150 or 200 mg/m^2 (60 min intravenous infusion) daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

Reporting group values	Non-Small Cell Lung Cancer (NSCLC): CAP7.1	Non-Small Cell Lung Cancer (NSCLC): Best Supportive Care (BSC)	Small Cell Lung Cancer (SCLC): CAP7.1
Number of subjects	4	4	8
Age categorical Units: Subjects			
Adults (18-64 years)	2	2	3
From 65-84 years	2	2	5

Age continuous			
Units: years			
arithmetic mean	63.0	61.5	63.3
standard deviation	± 4.08	± 11.00	± 8.15
Gender categorical			
Units: Subjects			
Female	2	1	1
Male	2	3	7

Reporting group values	Biliary tract cancer: CAP7.1	Biliary tract cancer: Best Supportive Care (BSC)	Total
Number of subjects	14	13	43
Age categorical			
Units: Subjects			
Adults (18-64 years)	9	6	22
From 65-84 years	5	7	21
Age continuous			
Units: years			
arithmetic mean	60.3	65.8	
standard deviation	± 10.54	± 8.70	-
Gender categorical			
Units: Subjects			
Female	6	7	17
Male	8	6	26

End points

End points reporting groups

Reporting group title	Non-Small Cell Lung Cancer (NSCLC): CAP7.1

Reporting group description:

Subjects with NSCLC who had progressed despite previous therapies received 60 minutes (min) intravenous infusion of 150 or 200 milligram per square meter (mg/m^2) CAP7.1 daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

Reporting group title	Non-Small Cell Lung Cancer (NSCLC): Best Supportive Care (BSC)

Reporting group description:

Subjects with NSCLC who had progressed despite previous therapies received best support as per institutional standards. In case of progression, these subjects were allowed to cross over to CAP7.1 therapy at the dose of 150 or 200 mg/m^2 (60 min intravenous infusion) daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

Reporting group title	Small Cell Lung Cancer (SCLC): CAP7.1

Reporting group description:

Subjects with SCLC who had progressed despite previous therapies received 60 min intravenous infusion of 150 or 200 mg/m^2 CAP7.1 daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

Reporting group title	Biliary tract cancer: CAP7.1

Reporting group description:

Subjects with advanced biliary tract cancer who had progressed despite previous therapies received 60 min intravenous infusion of 150 or 200 mg/m^2 CAP7.1 daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

Reporting group title	Biliary tract cancer: Best Supportive Care (BSC)

Reporting group description:

Subjects with advanced biliary tract cancer who had progressed despite previous therapies received best support as per institutional standards. In case of progression, these subjects were allowed to cross over to CAP7.1 therapy at the dose of 150 or 200 mg/m^2 (60 min intravenous infusion) daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

Primary: Percentage of Subjects With Disease Control

End point title	Percentage of Subjects With Disease Control

End point description:

The rate of disease control was defined as the percentage of subjects who have achieved complete, partial remission and stable disease (CR+PR+SD), according to RECIST 1.1. CR was defined as disappearance of all target lesions/ disappearance of all non-target lesions and normalization of tumor marker level. PR was defined as at least a 30% decrease in the sum of the limited-stage disease (LD) of target lesions, taking as reference the baseline sum LD. SD was defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease (PD), taking as reference the smallest sum LD since the treatment started. PD was defined as at least a 20% increase in the sum of the LD of target lesions, taking as reference the smallest sum LD recorded since the treatment started or the appearance of one or more new lesions/appearance of one or more new lesions and/or

unequivocal progression of existing non-target lesions.

End point type	Primary

End point timeframe:

Start of study treatment until 30 days post-last study treatment (approximately 2 years and 9 months)

End point values	Non-Small Cell Lung Cancer (NSCLC): CAP7.1	Non-Small Cell Lung Cancer (NSCLC): Best Supportive Care (BSC)	Small Cell Lung Cancer (SCLC): CAP7.1	Biliary tract cancer: CAP7.1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[1]	3[2]	8[3]	10[4]
Units: Percentage of subjects				
number (confidence interval 95%)	50.0 (6.8 to 93.2)	0.0 (0.0 to 70.8)	25.0 (3.2 to 65.1)	50.0 (18.7 to 81.3)

Notes:

[1] - Full analysis set (FAS) included all randomized subjects.

[2] - FAS with evaluable subjects for this end point.

[3] - FAS

[4] - FAS with evaluable subjects for this end point.

End point values	Biliary tract cancer: Best Supportive Care (BSC)			
Subject group type	Reporting group			
Number of subjects analysed	10[5]			
Units: Percentage of subjects				
number (confidence interval 95%)	20.0 (2.5 to 55.6)			

Notes:

[5] - FAS with evaluable subjects for this end point.

Statistical analyses

Statistical analysis title	Statistical analysis 1: NSCLC
Comparison groups	Non-Small Cell Lung Cancer (NSCLC): CAP7.1 v Non-Small Cell Lung Cancer (NSCLC): Best Supportive Care (BSC)
Number of subjects included in analysis	7
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.286
Method	t-test, 1-sided
Parameter estimate	Treatment difference
Point estimate	50
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.14
upper limit	93.24

Statistical analysis title	Statistical analysis 2: Biliary
Comparison groups	Biliary tract cancer: CAP7.1 v Biliary tract cancer: Best Supportive Care (BSC)
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.175
Method	t-test, 1-sided
Parameter estimate	Treatment difference
Point estimate	30
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.44
upper limit	69.22

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of study drug administration until 6 months post-therapy discontinuation/death

Adverse event reporting additional description:

The reporting groups "Biliary tract cancer: BSC before cross-over to CAP7.1" and "Biliary tract cancer: CAP7.1 after Best Supportive Care" were not mutually exclusive for the representation of adverse events.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0E

Reporting groups

Reporting group title	Non-Small Cell Lung Cancer (NSCLC): CAP7.1

Reporting group description:

Subjects with NSCLC who had progressed despite previous therapies received 60 minutes (min) intravenous infusion of 150 or 200 milligram per square meter (mg/m^2) CAP7.1 daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

Reporting group title	Non-Small Cell Lung Cancer (NSCLC): Best Supportive Care

Reporting group description:

Subjects with NSCLC who had progressed despite previous therapies received best support as per institutional standards. In case of progression, these subjects were allowed to cross over to CAP7.1 therapy at the dose of 150 or 200 mg/m^2 (60 min intravenous infusion) daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

Reporting group title	Small Cell Lung Cancer (SCLC): CAP7.1

Reporting group description:

Subjects with SCLC who had progressed despite previous therapies received 60 min intravenous infusion of 150 or 200 mg/m^2 CAP7.1 daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

Reporting group title	Biliary tract cancer: CAP7.1

Reporting group description:

Subjects with advanced biliary tract cancer who had progressed despite previous therapies received 60 min intravenous infusion of 150 or 200 mg/m^2 CAP7.1 daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

Reporting group title	Biliary tract cancer: BSC before cross-over to CAP7.1

Reporting group description:

Subjects with advanced biliary tract cancer who had progressed despite previous therapies received best support as per institutional standards. In case of progression, these subjects were allowed to cross over to CAP7.1 therapy at the dose of 150 or 200 mg/m^2 (60 min intravenous infusion) daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

Reporting group title	Biliary tract cancer: CAP7.1 after Best Supportive Care

Reporting group description:

Subjects with advanced biliary tract cancer who had progressed despite previous therapies received best

support as per institutional standards. In case of progression, these subjects were allowed to cross over to CAP7.1 therapy at the dose of 150 or 200 mg/m^2 (60 min intravenous infusion) daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

Serious adverse events	Non-Small Cell Lung Cancer (NSCLC): CAP7.1	Non-Small Cell Lung Cancer (NSCLC): Best Supportive Care	Small Cell Lung Cancer (SCLC): CAP7.1
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 4 (50.00%)	1 / 2 (50.00%)	6 / 8 (75.00%)
number of deaths (all causes)	4	2	8
number of deaths resulting from adverse events	1	0	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac tamponade			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematotoxicity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Condition aggravated			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0

Device occlusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disease progression			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	2 / 8 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
General physical health deterioration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion site anaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 2 (50.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			

Cholangitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice cholestatic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour lysis syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Biliary tract cancer: CAP7.1	Biliary tract cancer: BSC before cross-over to CAP7.1	Biliary tract cancer: CAP7.1 after Best Supportive Care
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 13 (53.85%)	2 / 10 (20.00%)	8 / 10 (80.00%)
number of deaths (all causes)	12	0	10
number of deaths resulting from adverse events	4	0	4
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac arrest			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac tamponade			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematotoxicity			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	2 / 13 (15.38%)	0 / 10 (0.00%)	3 / 10 (30.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	2 / 10 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Condition aggravated			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Death			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device occlusion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disease progression			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
General physical health deterioration			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Infusion site anaesthesia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	2 / 10 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	1 / 13 (7.69%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice cholestatic			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			

subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Febrile infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Urinary tract infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0

Tumour lysis syndrome			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0

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

Non-serious adverse events	Non-Small Cell Lung Cancer (NSCLC): CAP7.1	Non-Small Cell Lung Cancer (NSCLC): Best Supportive Care	Small Cell Lung Cancer (SCLC): CAP7.1
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	1 / 2 (50.00%)	8 / 8 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypertensive crisis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Microangiopathy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Central venous catheter removal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Resuscitation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	2 / 4 (50.00%)	0 / 2 (0.00%)	2 / 8 (25.00%)
occurrences (all)	2	0	2
Chills			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	3 / 4 (75.00%)	0 / 2 (0.00%)	5 / 8 (62.50%)
occurrences (all)	4	0	7
Feeling abnormal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
General physical health deterioration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Inflammation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Infusion site anaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Infusion site extravasation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Mucosal inflammation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pain			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Spinal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Breast swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pruritus genital			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	2
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	5 / 8 (62.50%)
occurrences (all)	0	0	5
Epistaxis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pharyngeal oedema			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Pulmonary embolism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Panic attack			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Stress			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
C-reactive protein increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Carbohydrate antigen 19-9 increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Carcinoembryonic antigen increased			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Coagulation time prolonged			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Eastern Cooperative Oncology Group performance status			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Eastern Cooperative Oncology Group performance status worsened			
subjects affected / exposed	0 / 4 (0.00%)	1 / 2 (50.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Scratch			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Arrhythmia supraventricular			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Atrial fibrillation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Bradycardia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Dizziness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Facial paresis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Neuralgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 4 (75.00%)	0 / 2 (0.00%)	3 / 8 (37.50%)
occurrences (all)	3	0	4
Bicytopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Eosinophilia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Febrile neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Leukocytosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Leukopenia			

subjects affected / exposed	2 / 4 (50.00%)	0 / 2 (0.00%)	4 / 8 (50.00%)
occurrences (all)	2	0	7
Lymphopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Monocytopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	2 / 4 (50.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	2	0	1
Reticulocytopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eye irritation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Ocular icterus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			

subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Breath odour			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Cheilitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	3 / 8 (37.50%)
occurrences (all)	1	0	5
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	3 / 8 (37.50%)
occurrences (all)	0	0	3
Dysphagia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia oral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	2 / 4 (50.00%)	0 / 2 (0.00%)	4 / 8 (50.00%)
occurrences (all)	2	0	6
Stomatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Vomiting			

subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	2
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hepatic pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypertransaminasaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Jaundice			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	2
Alopecia totalis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Decubitus ulcer			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Night sweats			

subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pruritus generalised			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Skin fissures			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Leukocyturia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Renal failure acute			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Renal impairment			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Bursitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Muscle twitching			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	3 / 8 (37.50%)
occurrences (all)	0	0	5
Pain in extremity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			

Administration site infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Candidiasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Oral candidiasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Oral fungal infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Periodontitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Sepsis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Vulvitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	2 / 4 (50.00%)	0 / 2 (0.00%)	5 / 8 (62.50%)
occurrences (all)	2	0	8
Hyperkalaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hyperphosphataemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hyperphosphatasaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Hypocalcaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Biliary tract cancer: CAP7.1	Biliary tract cancer: BSC before cross-over to CAP7.1	Biliary tract cancer: CAP7.1 after Best Supportive Care
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 13 (100.00%)	8 / 10 (80.00%)	10 / 10 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Hypertensive crisis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hypotension			

subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Microangiopathy			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Surgical and medical procedures			
Central venous catheter removal			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Resuscitation			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 13 (7.69%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
Chest discomfort			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Chest pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Chills			
subjects affected / exposed	2 / 13 (15.38%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	1
Fatigue			
subjects affected / exposed	4 / 13 (30.77%)	0 / 10 (0.00%)	4 / 10 (40.00%)
occurrences (all)	6	0	4
Feeling abnormal			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
General physical health deterioration			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Inflammation			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infusion site anaesthesia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Infusion site extravasation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Oedema			
subjects affected / exposed	2 / 13 (15.38%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	1
Oedema peripheral			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	3
Pain			
subjects affected / exposed	2 / 13 (15.38%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	3	0	0
Pyrexia			
subjects affected / exposed	1 / 13 (7.69%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
Spinal pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Breast swelling			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pruritus genital			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Vaginal haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 13 (15.38%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	2	1	0
Dyspnoea			
subjects affected / exposed	2 / 13 (15.38%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	1
Epistaxis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Oropharyngeal pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Pharyngeal oedema			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pleural effusion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Insomnia			

subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Panic attack			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Stress			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Investigations			
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Carbohydrate antigen 19-9 increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Carcinoembryonic antigen increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Coagulation time prolonged			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eastern Cooperative Oncology Group performance status			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Eastern Cooperative Oncology Group performance status worsened			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			

Fall			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Scratch			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Arrhythmia supraventricular			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Bradycardia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Aphasia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	1 / 13 (7.69%)	1 / 10 (10.00%)	2 / 10 (20.00%)
occurrences (all)	1	1	2
Facial paresis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	1
Neuralgia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Tremor			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 13 (53.85%)	1 / 10 (10.00%)	5 / 10 (50.00%)
occurrences (all)	20	1	13
Bicytopenia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Eosinophilia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Febrile neutropenia			
subjects affected / exposed	2 / 13 (15.38%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Leukocytosis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Leukopenia			
subjects affected / exposed	10 / 13 (76.92%)	0 / 10 (0.00%)	5 / 10 (50.00%)
occurrences (all)	25	0	7
Lymphopenia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Monocytopenia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Neutropenia			
subjects affected / exposed	7 / 13 (53.85%)	0 / 10 (0.00%)	7 / 10 (70.00%)
occurrences (all)	17	0	13
Reticulocytopenia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Thrombocytopenia			
subjects affected / exposed	7 / 13 (53.85%)	0 / 10 (0.00%)	5 / 10 (50.00%)
occurrences (all)	21	0	7

Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	2
Eye disorders			
Eye irritation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Ocular icterus			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Visual impairment			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	4 / 13 (30.77%)	2 / 10 (20.00%)	1 / 10 (10.00%)
occurrences (all)	5	2	1
Abdominal pain upper			
subjects affected / exposed	2 / 13 (15.38%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	3	0	1
Ascites			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	2
Breath odour			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Cheilitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	2 / 13 (15.38%)	0 / 10 (0.00%)	4 / 10 (40.00%)
occurrences (all)	2	0	4
Diarrhoea			

subjects affected / exposed	5 / 13 (38.46%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	5	0	1
Dysphagia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	2 / 13 (15.38%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	2	1	0
Hypoaesthesia oral			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	4 / 13 (30.77%)	1 / 10 (10.00%)	2 / 10 (20.00%)
occurrences (all)	6	1	2
Stomatitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	1 / 13 (7.69%)	1 / 10 (10.00%)	2 / 10 (20.00%)
occurrences (all)	1	1	2
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hepatic pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Hyperbilirubinaemia			
subjects affected / exposed	2 / 13 (15.38%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	3	0	1
Hypertransaminasaemia			
subjects affected / exposed	2 / 13 (15.38%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	5	0	0
Jaundice			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0

Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	4 / 13 (30.77%)	0 / 10 (0.00%)	4 / 10 (40.00%)
occurrences (all)	4	0	4
Alopecia totalis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Decubitus ulcer			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Dry skin			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Night sweats			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Pruritus generalised			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	3 / 10 (30.00%)
occurrences (all)	0	1	4
Rash pruritic			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin fissures			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Skin hyperpigmentation			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Skin lesion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Leukocyturia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Proteinuria			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Renal failure acute			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Renal impairment			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 13 (7.69%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	1	1	2
Back pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Bone pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Bursitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Flank pain			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Muscle twitching			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Musculoskeletal pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Infections and infestations			
Administration site infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Candidiasis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Oral candidiasis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Oral fungal infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Periodontitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1

Pharyngitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Sepsis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Vulvitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 13 (23.08%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	3	1	1
Hyperkalaemia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hyperphosphataemia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hyperphosphatasaemia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	2
Hyperuricaemia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Hypoalbuminaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			

subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hyponatraemia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 November 2013	- Tissue sampling with MRT and Ultrasound was added. - Dose adjustment
27 February 2014	- MRT removed

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 study was terminated to be redesigned for a trial according to EMA proposal.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28531881