



Clinical trial results:

Phase III study comparing the efficacy of paclitaxel-bevacizumab with docetaxel in 2nd or 3rd line of treatment of non squamous Non Small Cell Lung Cancer

Summary

EudraCT number	2012-004524-38
Trial protocol	FR
Global end of trial date	12 April 2017

Results information

Result version number	v2 (current)
This version publication date	11 February 2022
First version publication date	08 April 2021
Version creation reason	• Correction of full data set SAEs update

Trial information

Trial identification

Sponsor protocol code	IFCT-1103 Ultimate
-----------------------	--------------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01763671
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	IFCT
Sponsor organisation address	10 rue de la Grange-Batelière, PARIS, France, 75009
Public contact	Responsable communication, IFCT, 33 156811046, contact@ifct.fr
Scientific contact	Responsable communication, IFCT, 33 156811046, contact@ifct.fr

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	29 June 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 April 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Progression free survival

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 May 2013
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	France: 166
Worldwide total number of subjects	166
EEA total number of subjects	166

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)	117
From 65 to 84 years	49
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 166 randomised patients [Paclitaxel-Bevacizumab group: 111 (67%), Docetaxel group: 55 (33%)] was included between May 31, 2013 and August 13, 2014.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	166
Number of subjects completed	166

Period 1

Period 1 title	Sequence 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A - Docetaxel (DOC)

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Docetaxel 75 mg/m² every 21 days

Arm title	Arm B - Paclitaxel plus bevacizumab (wPAC-BEV)
------------------	--

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

paclitaxel 90 mg/m² D1, D8, D15 every 28 days

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

Dosage and administration details:

bevacizumab 10 mg/kg D1, D15 every 28 days

Number of subjects in period 1	Arm A - Docetaxel (DOC)	Arm B - Paclitaxel plus bevacizumab (wPAC-BEV)
Started	55	111
Completed	55	109
Not completed	0	2
Physician decision	-	1
Disease progression	-	1

Period 2

Period 2 title	Sequence 2 (Cross-Over)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm B1 - Paclitaxel plus bevacizumab (cross-over)

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

paclitaxel 90 mg/m² D1, D8, D15 every 28 days

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

Dosage and administration details:

bevacizumab 10 mg/kg D1, D15 every 28 days

Arm title	Arm A1 - Docetaxel (cross-over)
------------------	---------------------------------

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:
Docetaxel 75 mg/m² every 21 days

Number of subjects in period 2 ^[1]	Arm B1 - Paclitaxel plus bevacizumab (cross-over)	Arm A1 - Docetaxel (cross-over)
Started	21	9
Completed	21	9

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: The cross-over was optional

Baseline characteristics

Reporting groups

Reporting group title	Arm A - Docetaxel (DOC)
Reporting group description: -	
Reporting group title	Arm B - Paclitaxel plus bevacizumab (wPAC-BEV)
Reporting group description: -	

Reporting group values	Arm A - Docetaxel (DOC)	Arm B - Paclitaxel plus bevacizumab (wPAC-BEV)	Total
Number of subjects	55	111	166
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	60.74	59.57	
standard deviation	± 9.44	± 9.38	-
Gender categorical			
Units: Subjects			
Female	13	78	91
Male	42	33	75
Smoking			
Units: Subjects			
No	9	9	18
Yes	46	102	148
PS			
Units: Subjects			
PS 0	20	47	67
PS 1	31	56	87
PS 2	4	8	12
Histology			
Units: Subjects			
Adenocarcinoma	51	100	151
Large cells/No	4	11	15
Previous exposure to bevacizumab			
Units: Subjects			
No	38	77	115
Yes	17	34	51

Number of previous lines Units: Subjects			
1 line	39	76	115
2 lines	14	34	48
3 lines	2	1	3
Time between the diagnostic of cancer and inclusion Units: Subjects			
< 9 months	20	52	72
> 9 months	35	59	94
Age class Units: Subjects			
< 70 years old	45	101	146
> 70 years old	10	10	20
Weight loss Units: Subjects			
< 0 kg	12	20	32
0 - 5 kg	42	85	127
5 - 10 kg	1	4	5
missing	0	2	2
EGFR Units: Subjects			
Activating mutation	2	4	6
Resistance mutation	1	0	1
Other mutation	0	1	1
Wild-type	44	87	131
Inderminate	5	9	14
Not done	3	10	13
Weight Units: kilogram(s)			
arithmetic mean	69.18	69.05	
standard deviation	± 12.47	± 13.72	-
Number of pack-year Units: pack-years			
arithmetic mean	44.11	37.38	
standard deviation	± 23.54	± 21.40	-

End points

End points reporting groups

Reporting group title	Arm A - Docetaxel (DOC)
Reporting group description: -	
Reporting group title	Arm B - Paclitaxel plus bevacizumab (wPAC-BEV)
Reporting group description: -	
Reporting group title	Arm B1 - Paclitaxel plus bevacizumab (cross-over)
Reporting group description: -	
Reporting group title	Arm A1 - Docetaxel (cross-over)
Reporting group description: -	

Primary: Progression free survival

End point title	Progression free survival
End point description:	
End point type	Primary
End point timeframe:	
Time between randomisation and disease progression (as assessed by the investigator using RECIST 1.1) or death from any cause, whatever came first.	

End point values	Arm A - Docetaxel (DOC)	Arm B - Paclitaxel plus bevacizumab (wPAC-BEV)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	109		
Units: months				
number (confidence interval 95%)	3.9 (2.69 to 5.26)	5.4 (4.63 to 7.13)		

Statistical analyses

Statistical analysis title	Progression Free Survival
Statistical analysis description:	
Time between randomisation and disease progression (as assessed by the investigator using RECIST 1.1) or death from any cause, whatever came first.	
Comparison groups	Arm A - Docetaxel (DOC) v Arm B - Paclitaxel plus bevacizumab (wPAC-BEV)

Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	0.86

Secondary: Response Rate

End point title	Response Rate
End point description:	
End point type	Secondary
End point timeframe:	
At 8 weeks	

End point values	Arm A - Docetaxel (DOC)	Arm B - Paclitaxel plus bevacizumab (wPAC-BEV)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	109		
Units: Pourcentage				
Not Done / Not Evaluable	4	10		
Progression	19	21		
Objective response	3	25		
Stable	29	55		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival
End point description:	
End point type	Secondary
End point timeframe:	
Overall survival is defined as time between date of inclusion and all-cause death	

End point values	Arm A - Docetaxel (DOC)	Arm B - Paclitaxel plus bevacizumab (wPAC-BEV)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	109		
Units: months				
number (confidence interval 95%)	11.4 (7.85 to 13.14)	9.9 (8.11 to 12.2)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The adverse events have to be reported from inclusion to 30 day following the end of administration of study treatments.

Assessment type	Non-systematic
-----------------	----------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	18
--------------------	----

Reporting groups

Reporting group title	Safety population - Arm A
-----------------------	---------------------------

Reporting group description:

The safety population - Arm A will be defined as all patients who received at least one dose of docetaxel.

Reporting group title	Safety population - Arm B
-----------------------	---------------------------

Reporting group description:

The safety population - Arm B will be defined as all patients who received at least one dose of paclitaxel and bevacizumab.

Reporting group title	Safety population - Arm A1
-----------------------	----------------------------

Reporting group description:

The safety population - Arm A1 will be defined as all patients who received at least one dose of docetaxel during cross-over.

Reporting group title	Safety population - Arm B1
-----------------------	----------------------------

Reporting group description:

The safety population - Arm B1 will be defined as all patients who received at least one dose of paclitaxel-bevacizumab during cross-over.

Serious adverse events	Safety population - Arm A	Safety population - Arm B	Safety population - Arm A1
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 55 (16.36%)	15 / 109 (13.76%)	5 / 9 (55.56%)
number of deaths (all causes)	32	94	9
number of deaths resulting from adverse events	3	2	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Carcinomatous peritonitis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 109 (0.00%)	0 / 9 (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
Meningeal carcinomatosis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 109 (0.00%)	0 / 9 (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
Progression of bronchial carcinoma			

subjects affected / exposed	3 / 55 (5.45%)	2 / 109 (1.83%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 0
Vascular disorders			
Esophagitis hemorrhagic			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (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
Superior vena cava syndrome			
subjects affected / exposed	1 / 55 (1.82%)	0 / 109 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fever			
subjects affected / exposed	2 / 55 (3.64%)	5 / 109 (4.59%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 2	2 / 5	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Reduced general condition			
subjects affected / exposed	6 / 55 (10.91%)	12 / 109 (11.01%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	2 / 6	8 / 12	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	1 / 55 (1.82%)	3 / 109 (2.75%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chills			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (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

Death			
subjects affected / exposed	0 / 55 (0.00%)	2 / 109 (1.83%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Fatigue			
subjects affected / exposed	1 / 55 (1.82%)	0 / 109 (0.00%)	0 / 9 (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
Malaise			
subjects affected / exposed	1 / 55 (1.82%)	0 / 109 (0.00%)	0 / 9 (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	1 / 55 (1.82%)	1 / 109 (0.92%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Immune system disorders			
Drug allergy			
subjects affected / exposed	0 / 55 (0.00%)	2 / 109 (1.83%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Dyspnea			
subjects affected / exposed	0 / 55 (0.00%)	6 / 109 (5.50%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Respiratory, thoracic and mediastinal disorders			
Esophagobronchial fistula			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Hypoxia			

subjects affected / exposed	1 / 55 (1.82%)	2 / 109 (1.83%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 1	0 / 0
Interstitial pneumonitis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumopathy			
subjects affected / exposed	2 / 55 (3.64%)	4 / 109 (3.67%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	3 / 3	3 / 3	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 1	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 55 (1.82%)	3 / 109 (2.75%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 55 (0.00%)	5 / 109 (4.59%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 55 (0.00%)	2 / 109 (1.83%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Acute respiratory failure			
subjects affected / exposed	2 / 55 (3.64%)	0 / 109 (0.00%)	0 / 9 (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
Exertional dyspnea			
subjects affected / exposed	1 / 55 (1.82%)	0 / 109 (0.00%)	0 / 9 (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
Pleural effusion			

subjects affected / exposed	0 / 55 (0.00%)	2 / 109 (1.83%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Investigations			
Neutrophil count decreased			
subjects affected / exposed	2 / 55 (3.64%)	0 / 109 (0.00%)	0 / 9 (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
Hemoglobin decreased			
subjects affected / exposed	1 / 55 (1.82%)	0 / 109 (0.00%)	0 / 9 (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
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Pericarditis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (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
Supraventricular tachycardia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 109 (0.00%)	0 / 9 (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
Nervous system disorders			
Confusion			
subjects affected / exposed	1 / 55 (1.82%)	0 / 109 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy			
subjects affected / exposed	0 / 55 (0.00%)	2 / 109 (1.83%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stroke			
subjects affected / exposed	0 / 55 (0.00%)	3 / 109 (2.75%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Balance disorder			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Convulsion			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (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
Epilepsy			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (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
Intracranial hypertension			

subjects affected / exposed	1 / 55 (1.82%)	0 / 109 (0.00%)	0 / 9 (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
Loss of consciousness			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (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
Memory impairment			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Motor activity retarded			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (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
Neuralgia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 109 (0.00%)	0 / 9 (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
Neurological disorder NOS			
subjects affected / exposed	0 / 55 (0.00%)	2 / 109 (1.83%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 109 (0.00%)	0 / 9 (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
Aplasia bone marrow			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile aplasia			

subjects affected / exposed	1 / 55 (1.82%)	0 / 109 (0.00%)	0 / 9 (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
Febrile neutropenia			
subjects affected / exposed	2 / 55 (3.64%)	0 / 109 (0.00%)	0 / 9 (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
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 55 (0.00%)	2 / 109 (1.83%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 55 (0.00%)	0 / 109 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Dysphagia			
subjects affected / exposed	1 / 55 (1.82%)	1 / 109 (0.92%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Esophagitis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (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
Gastralgia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 109 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematemesis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Intestinal obstruction			

subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (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
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (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
Hepatic cytolysis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Skin and subcutaneous tissue disorders			
Hand-and-foot syndrome			
subjects affected / exposed	1 / 55 (1.82%)	0 / 109 (0.00%)	0 / 9 (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
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 55 (1.82%)	0 / 109 (0.00%)	0 / 9 (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
Musculoskeletal and connective tissue disorders			
Fracture NOS			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	3 / 55 (5.45%)	2 / 109 (1.83%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in hip			

subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (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
Shoulder pain			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (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
Tendinitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 109 (0.00%)	0 / 9 (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
Bone pain			
subjects affected / exposed	0 / 55 (0.00%)	0 / 109 (0.00%)	2 / 9 (22.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Catheter related infection			
subjects affected / exposed	0 / 55 (0.00%)	3 / 109 (2.75%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection NOS			
subjects affected / exposed	1 / 55 (1.82%)	1 / 109 (0.92%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Oral candida			
subjects affected / exposed	0 / 55 (0.00%)	0 / 109 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural infection			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystosis			

subjects affected / exposed	1 / 55 (1.82%)	0 / 109 (0.00%)	0 / 9 (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
Sepsis			
subjects affected / exposed	1 / 55 (1.82%)	2 / 109 (1.83%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (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
Bronchitis			
subjects affected / exposed	0 / 55 (0.00%)	2 / 109 (1.83%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site infection			
subjects affected / exposed	1 / 55 (1.82%)	0 / 109 (0.00%)	0 / 9 (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
Colonic abscess			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (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
Localized infection			
subjects affected / exposed	0 / 55 (0.00%)	2 / 109 (1.83%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (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
Respiratory infection			

subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anorexia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (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
Diabetes			
subjects affected / exposed	1 / 55 (1.82%)	0 / 109 (0.00%)	0 / 9 (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
Hypercalcemia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (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
Hyperglycemia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (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
Malnutrition			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	0 / 9 (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

Serious adverse events	Safety population - Arm B1		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 21 (14.29%)		
number of deaths (all causes)	17		
number of deaths resulting from adverse events	0		

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Carcinomatous peritonitis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Meningeal carcinomatosis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Progression of bronchial carcinoma			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Esophagitis hemorrhagic			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Orthostatic hypotension			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Superior vena cava syndrome			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fever			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reduced general condition			

subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Chest pain			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chills			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Death			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malaise			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pain			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Drug allergy			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			

Dyspnea			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Esophagobronchial fistula			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoxia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Interstitial pneumonitis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumopathy			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Acute respiratory failure			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Exertional dyspnea			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory distress			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Neutrophil count decreased			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hemoglobin decreased			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Arrhythmia			

subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pericarditis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Supraventricular tachycardia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Confusion			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neuropathy			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Stroke			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Balance disorder			

subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Convulsion				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intracranial hypertension				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Loss of consciousness				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Memory impairment				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Motor activity retarded				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neuralgia				
subjects affected / exposed	1 / 21 (4.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neurological disorder NOS				

subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Aplasia bone marrow			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile aplasia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dysphagia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Esophagitis			

subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastralgia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haematemesis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic cytolysis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Hand-and-foot syndrome			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Musculoskeletal and connective tissue disorders			
Fracture NOS			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pain in hip			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Shoulder pain			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tendinitis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bone pain			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Catheter related infection			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infection NOS			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Oral candida				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural infection				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumocystosis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 21 (4.76%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Abscess				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Catheter site infection				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colonic abscess				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Localized infection				

subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Meningitis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory infection			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anorexia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diabetes			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypercalcemia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperglycemia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malnutrition			

subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Safety population - Arm A	Safety population - Arm B	Safety population - Arm A1
Total subjects affected by non-serious adverse events			
subjects affected / exposed	54 / 55 (98.18%)	109 / 109 (100.00%)	9 / 9 (100.00%)
Vascular disorders			
Epistaxis			
subjects affected / exposed	2 / 55 (3.64%)	47 / 109 (43.12%)	0 / 9 (0.00%)
occurrences (all)	5	81	0
Hypertension			
subjects affected / exposed	0 / 55 (0.00%)	24 / 109 (22.02%)	1 / 9 (11.11%)
occurrences (all)	0	33	1
Pulmonary embolism			
subjects affected / exposed	1 / 55 (1.82%)	8 / 109 (7.34%)	0 / 9 (0.00%)
occurrences (all)	1	15	0
Haemoptysis			
subjects affected / exposed	3 / 55 (5.45%)	6 / 109 (5.50%)	0 / 9 (0.00%)
occurrences (all)	5	7	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	30 / 55 (54.55%)	65 / 109 (59.63%)	2 / 9 (22.22%)
occurrences (all)	70	145	2
Oedema peripheral			
subjects affected / exposed	5 / 55 (9.09%)	16 / 109 (14.68%)	0 / 9 (0.00%)
occurrences (all)	8	20	0
Fatigue			
subjects affected / exposed	2 / 55 (3.64%)	5 / 109 (4.59%)	1 / 9 (11.11%)
occurrences (all)	3	7	1
General physical health deterioration			
subjects affected / exposed	9 / 55 (16.36%)	8 / 109 (7.34%)	3 / 9 (33.33%)
occurrences (all)	9	9	3

Oedema			
subjects affected / exposed	0 / 55 (0.00%)	1 / 109 (0.92%)	1 / 9 (11.11%)
occurrences (all)	0	2	1
Diarrhoea			
subjects affected / exposed	13 / 55 (23.64%)	26 / 109 (23.85%)	1 / 9 (11.11%)
occurrences (all)	23	38	1
Chest pain			
subjects affected / exposed	7 / 55 (12.73%)	10 / 109 (9.17%)	1 / 9 (11.11%)
occurrences (all)	13	13	1
Pyrexia			
subjects affected / exposed	6 / 55 (10.91%)	7 / 109 (6.42%)	1 / 9 (11.11%)
occurrences (all)	7	9	1
Face oedema			
subjects affected / exposed	3 / 55 (5.45%)	0 / 109 (0.00%)	0 / 9 (0.00%)
occurrences (all)	3	0	0
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	1 / 55 (1.82%)	13 / 109 (11.93%)	0 / 9 (0.00%)
occurrences (all)	1	22	0
Dyspnoea			
subjects affected / exposed	16 / 55 (29.09%)	25 / 109 (22.94%)	2 / 9 (22.22%)
occurrences (all)	27	42	2
Lung disorder			
subjects affected / exposed	2 / 55 (3.64%)	3 / 109 (2.75%)	1 / 9 (11.11%)
occurrences (all)	3	3	1
Cough			
subjects affected / exposed	17 / 55 (30.91%)	31 / 109 (28.44%)	2 / 9 (22.22%)
occurrences (all)	29	70	2
Dyspnoea exertional			
subjects affected / exposed	4 / 55 (7.27%)	5 / 109 (4.59%)	0 / 9 (0.00%)
occurrences (all)	7	8	0
Productive cough			
subjects affected / exposed	4 / 55 (7.27%)	5 / 109 (4.59%)	0 / 9 (0.00%)
occurrences (all)	5	8	0
Pneumothorax			

subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 1	3 / 109 (2.75%) 5	0 / 9 (0.00%) 0
Pulmonary congestion subjects affected / exposed occurrences (all)	2 / 55 (3.64%) 2	0 / 109 (0.00%) 0	0 / 9 (0.00%) 0
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 1	7 / 109 (6.42%) 8	0 / 9 (0.00%) 0
Investigations Weight decreased subjects affected / exposed occurrences (all)	9 / 55 (16.36%) 10	16 / 109 (14.68%) 18	2 / 9 (22.22%) 2
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	6 / 55 (10.91%) 15	13 / 109 (11.93%) 18	2 / 9 (22.22%) 2
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	2 / 55 (3.64%) 3	6 / 109 (5.50%) 8	2 / 9 (22.22%) 2
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	2 / 55 (3.64%) 2	8 / 109 (7.34%) 12	0 / 9 (0.00%) 0
Nervous system disorders Paraesthesia subjects affected / exposed occurrences (all)	10 / 55 (18.18%) 25	40 / 109 (36.70%) 72	3 / 9 (33.33%) 3
Neuropathy peripheral subjects affected / exposed occurrences (all)	5 / 55 (9.09%) 10	22 / 109 (20.18%) 60	0 / 9 (0.00%) 0
Dysgeusia subjects affected / exposed occurrences (all)	2 / 55 (3.64%) 2	8 / 109 (7.34%) 13	0 / 9 (0.00%) 0
Hypoaesthesia subjects affected / exposed occurrences (all)	3 / 55 (5.45%) 6	0 / 109 (0.00%) 0	0 / 9 (0.00%) 0
Headache			

subjects affected / exposed occurrences (all)	6 / 55 (10.91%) 6	14 / 109 (12.84%) 21	1 / 9 (11.11%) 1
Sciatica subjects affected / exposed occurrences (all)	3 / 55 (5.45%) 5	3 / 109 (2.75%) 4	0 / 9 (0.00%) 0
Confusional state subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 1	1 / 109 (0.92%) 1	2 / 9 (22.22%) 2
Monoparesis subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 109 (0.00%) 0	2 / 9 (22.22%) 2
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	40 / 55 (72.73%) 119	67 / 109 (61.47%) 144	6 / 9 (66.67%) 6
Neutropenia subjects affected / exposed occurrences (all)	31 / 55 (56.36%) 68	50 / 109 (45.87%) 110	4 / 9 (44.44%) 6
Thrombocytopenia subjects affected / exposed occurrences (all)	13 / 55 (23.64%) 19	13 / 109 (11.93%) 25	1 / 9 (11.11%) 1
Febrile neutropenia subjects affected / exposed occurrences (all)	4 / 55 (7.27%) 4	1 / 109 (0.92%) 1	0 / 9 (0.00%) 0
Febrile bone marrow aplasia subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 109 (0.00%) 0	1 / 9 (11.11%) 1
Ear and labyrinth disorders			
Vertigo subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 1	7 / 109 (6.42%) 10	0 / 9 (0.00%) 0
Eye disorders			
Lacrimation increased subjects affected / exposed occurrences (all)	3 / 55 (5.45%) 6	1 / 109 (0.92%) 3	0 / 9 (0.00%) 0
Gastrointestinal disorders			

Nausea			
subjects affected / exposed	13 / 55 (23.64%)	28 / 109 (25.69%)	1 / 9 (11.11%)
occurrences (all)	15	43	1
Stomatitis			
subjects affected / exposed	5 / 55 (9.09%)	21 / 109 (19.27%)	1 / 9 (11.11%)
occurrences (all)	5	31	1
Constipation			
subjects affected / exposed	4 / 55 (7.27%)	28 / 109 (25.69%)	1 / 9 (11.11%)
occurrences (all)	4	36	1
Vomiting			
subjects affected / exposed	7 / 55 (12.73%)	20 / 109 (18.35%)	0 / 9 (0.00%)
occurrences (all)	7	27	0
Abdominal pain			
subjects affected / exposed	5 / 55 (9.09%)	6 / 109 (5.50%)	0 / 9 (0.00%)
occurrences (all)	8	8	0
Abdominal pain upper			
subjects affected / exposed	0 / 55 (0.00%)	9 / 109 (8.26%)	2 / 9 (22.22%)
occurrences (all)	0	12	2
Subileus			
subjects affected / exposed	0 / 55 (0.00%)	0 / 109 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	19 / 55 (34.55%)	32 / 109 (29.36%)	1 / 9 (11.11%)
occurrences (all)	36	57	1
Nail disorder			
subjects affected / exposed	1 / 55 (1.82%)	5 / 109 (4.59%)	0 / 9 (0.00%)
occurrences (all)	2	12	0
Onycholysis			
subjects affected / exposed	0 / 55 (0.00%)	4 / 109 (3.67%)	0 / 9 (0.00%)
occurrences (all)	0	8	0
Dry skin			
subjects affected / exposed	2 / 55 (3.64%)	6 / 109 (5.50%)	0 / 9 (0.00%)
occurrences (all)	6	13	0
Erythema			

subjects affected / exposed occurrences (all)	4 / 55 (7.27%) 6	4 / 109 (3.67%) 7	0 / 9 (0.00%) 0
Rash subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 1	4 / 109 (3.67%) 6	0 / 9 (0.00%) 0
Rash erythematous subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 109 (0.00%) 0	1 / 9 (11.11%) 1
Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	23 / 109 (21.10%) 49	0 / 9 (0.00%) 0
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	6 / 55 (10.91%) 10	19 / 109 (17.43%) 36	1 / 9 (11.11%) 1
Arthralgia subjects affected / exposed occurrences (all)	6 / 55 (10.91%) 14	15 / 109 (13.76%) 29	1 / 9 (11.11%) 1
Pain in extremity subjects affected / exposed occurrences (all)	5 / 55 (9.09%) 6	7 / 109 (6.42%) 9	0 / 9 (0.00%) 0
Musculoskeletal chest pain subjects affected / exposed occurrences (all)	4 / 55 (7.27%) 5	6 / 109 (5.50%) 6	0 / 9 (0.00%) 0
Bone pain subjects affected / exposed occurrences (all)	3 / 55 (5.45%) 3	5 / 109 (4.59%) 5	1 / 9 (11.11%) 1
Musculoskeletal pain subjects affected / exposed occurrences (all)	2 / 55 (3.64%) 3	6 / 109 (5.50%) 8	0 / 9 (0.00%) 0
Neck pain subjects affected / exposed occurrences (all)	2 / 55 (3.64%) 2	3 / 109 (2.75%) 4	1 / 9 (11.11%) 1
Musculoskeletal stiffness			

subjects affected / exposed	4 / 55 (7.27%)	0 / 109 (0.00%)	0 / 9 (0.00%)
occurrences (all)	5	0	0
Amyotrophy			
subjects affected / exposed	0 / 55 (0.00%)	0 / 109 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Infections and infestations			
Paronychia			
subjects affected / exposed	0 / 55 (0.00%)	4 / 109 (3.67%)	1 / 9 (11.11%)
occurrences (all)	0	5	1
Oral candidiasis			
subjects affected / exposed	2 / 55 (3.64%)	4 / 109 (3.67%)	1 / 9 (11.11%)
occurrences (all)	2	4	1
Bronchitis			
subjects affected / exposed	6 / 55 (10.91%)	10 / 109 (9.17%)	0 / 9 (0.00%)
occurrences (all)	6	10	0
Nasopharyngitis			
subjects affected / exposed	1 / 55 (1.82%)	7 / 109 (6.42%)	0 / 9 (0.00%)
occurrences (all)	1	15	0
Rhinitis			
subjects affected / exposed	2 / 55 (3.64%)	6 / 109 (5.50%)	0 / 9 (0.00%)
occurrences (all)	3	15	0
Lung infection			
subjects affected / exposed	1 / 55 (1.82%)	6 / 109 (5.50%)	0 / 9 (0.00%)
occurrences (all)	1	6	0
Urinary tract infection			
subjects affected / exposed	1 / 55 (1.82%)	6 / 109 (5.50%)	0 / 9 (0.00%)
occurrences (all)	1	7	0
Tooth abscess			
subjects affected / exposed	1 / 55 (1.82%)	5 / 109 (4.59%)	0 / 9 (0.00%)
occurrences (all)	1	6	0
Conjunctivitis			
subjects affected / exposed	3 / 55 (5.45%)	2 / 109 (1.83%)	0 / 9 (0.00%)
occurrences (all)	3	2	0
Infection			
subjects affected / exposed	3 / 55 (5.45%)	2 / 109 (1.83%)	1 / 9 (11.11%)
occurrences (all)	3	2	1

Metabolism and nutrition disorders			
Myalgia			
subjects affected / exposed	2 / 55 (3.64%)	9 / 109 (8.26%)	0 / 9 (0.00%)
occurrences (all)	4	20	0
Decreased appetite			
subjects affected / exposed	13 / 55 (23.64%)	27 / 109 (24.77%)	4 / 9 (44.44%)
occurrences (all)	29	41	5
Hypercreatinaemia			
subjects affected / exposed	11 / 55 (20.00%)	12 / 109 (11.01%)	1 / 9 (11.11%)
occurrences (all)	46	33	1
Hyperkalaemia			
subjects affected / exposed	2 / 55 (3.64%)	8 / 109 (7.34%)	0 / 9 (0.00%)
occurrences (all)	5	16	0
Hyperglycaemia			
subjects affected / exposed	0 / 55 (0.00%)	9 / 109 (8.26%)	1 / 9 (11.11%)
occurrences (all)	0	25	2
Hypoalbuminaemia			
subjects affected / exposed	1 / 55 (1.82%)	7 / 109 (6.42%)	1 / 9 (11.11%)
occurrences (all)	3	15	2
Hyponatraemia			
subjects affected / exposed	0 / 55 (0.00%)	3 / 109 (2.75%)	1 / 9 (11.11%)
occurrences (all)	0	6	1
Malnutrition			
subjects affected / exposed	1 / 55 (1.82%)	2 / 109 (1.83%)	1 / 9 (11.11%)
occurrences (all)	1	2	1

Non-serious adverse events	Safety population - Arm B1		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 21 (95.24%)		
Vascular disorders			
Epistaxis			
subjects affected / exposed	5 / 21 (23.81%)		
occurrences (all)	5		
Hypertension			
subjects affected / exposed	6 / 21 (28.57%)		
occurrences (all)	16		
Pulmonary embolism			

subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Haemoptysis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	9 / 21 (42.86%)		
occurrences (all)	28		
Oedema peripheral			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	2		
Fatigue			
subjects affected / exposed	4 / 21 (19.05%)		
occurrences (all)	4		
General physical health deterioration			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Oedema			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	4 / 21 (19.05%)		
occurrences (all)	4		
Chest pain			
subjects affected / exposed	4 / 21 (19.05%)		
occurrences (all)	5		
Pyrexia			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	3		
Face oedema			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			

Dysphonia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	6 / 21 (28.57%)		
occurrences (all)	10		
Lung disorder			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Cough			
subjects affected / exposed	4 / 21 (19.05%)		
occurrences (all)	7		
Dyspnoea exertional			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	3		
Productive cough			
subjects affected / exposed	4 / 21 (19.05%)		
occurrences (all)	6		
Pneumothorax			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	3		
Pulmonary congestion			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	4		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Investigations			
Weight decreased			
subjects affected / exposed	5 / 21 (23.81%)		
occurrences (all)	8		
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Blood alkaline phosphatase increased			

subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Alanine aminotransferase increased			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	4 / 21 (19.05%)		
occurrences (all)	5		
Neuropathy peripheral			
subjects affected / exposed	8 / 21 (38.10%)		
occurrences (all)	14		
Dysgeusia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Hypoaesthesia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	3		
Sciatica			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	4		
Confusional state			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Monoparesis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	16 / 21 (76.19%)		
occurrences (all)	30		
Neutropenia			

subjects affected / exposed	7 / 21 (33.33%)		
occurrences (all)	17		
Thrombocytopenia			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	3		
Febrile neutropenia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Febrile bone marrow aplasia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Eye disorders			
Lacrimation increased			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	5		
Stomatitis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	5		
Constipation			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	5		
Vomiting			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	4		
Abdominal pain upper			

subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Subileus			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	6		
Nail disorder			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	5		
Onycholysis			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	4		
Dry skin			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	3		
Erythema			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	2		
Rash			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	3		
Rash erythematous			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	2		
Arthralgia			

subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	4		
Pain in extremity			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	2		
Bone pain			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Neck pain			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Musculoskeletal stiffness			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Amyotrophy			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Paronychia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Oral candidiasis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		

Rhinitis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Lung infection			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	2		
Tooth abscess			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Conjunctivitis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Infection			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Myalgia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Decreased appetite			
subjects affected / exposed	7 / 21 (33.33%)		
occurrences (all)	16		
Hypercreatinaemia			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	5		
Hyperkalaemia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Hypoalbuminaemia			

subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Hyponatraemia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Malnutrition			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 May 2013	<ul style="list-style-type: none">- addition of an evaluation of the quality of life- reduction of the number of sites- addition of an inclusion criteria regarding the measurability of the disease- clarification of inclusion and exclusion criteria- clarification on the use of anticoagulation during the trial- deletion of the biological study

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.

Patients included in the DOC arm tended to be older and to be more frequently never smokers than in the paclitaxel-bavacizumab arm.
Cross-over from one arm to another prevented any definitive conclusion on OS benefit.

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/32276179>