Clinical trial results:
An Open-Label Phase I/IIa Study of Intravenous BAL101553 in Adult Patients with Advanced Solid Tumors

Summary

EudraCT number	2010-024237-23
Trial protocol	GB
Global end of trial date	06 April 2016

Results information

Result version number	v1 (current)
This version publication date	01 February 2019
First version publication date	01 February 2019

Trial information

Trial identification

Sponsor protocol code	CDI-CS-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01397929
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Basilea Pharmaceutica International Ltd.
Sponsor organisation address	Grenzacherstrasse 487, Basel, Switzerland,
Public contact	Medical Information, Basilea Pharmaceutical International Ltd., +41 6061400, medical.information@basilea.com
Scientific contact	Medical Information, Basilea Pharmaceutical International Ltd., +41 6061400, medical.information@basilea.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	07 February 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 April 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to determine the maximum tolerated dose (MTD) and to characterize dose-limiting toxicities (DLT) of BAL101553 administered intravenously as single agent on days 1, 8 and 15 of an every 28 day treatment cycle in adults with advanced or recurrent solid tumors, who have failed standard therapy or for whom no effective standard therapy is available

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice (GCP) and applicable national and regional regulations/guidelines regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 June 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 73
Worldwide total number of subjects	73
EEA total number of subjects	73

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)	50
From 65 to 84 years	23

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 4 Phase 1 study centers in the United Kingdom.

Pre-assignment

Screening details:

Total of 104 subjects were screened, out of which 25 subjects failed screening. Seventy-nine subjects were assigned to treatment of which 73 received at least one dose.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	BAL101553: 15 mg/m²

Arm description:

BAL101553 was administered at 15 mg/m² as an IV infusion over 2 hours on Days 1, 8 and 15 of a 28 day treatment Cycle. Treatment Cycles were continued until disease progression, unacceptable toxicity, or other discontinuation criteria met.

Arm type	Experimental
Investigational medicinal product name	BAL101553
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

BAL101553 15 mg/m² intravenously over 2 hours on Days 1, 8 and 15 of each 28-day treatment cycle.

Arm title	BAL101553: 30 mg/m²

Arm description:

BAL101553 was administered at 30 mg/m² as an IV infusion over 2 hours on Days 1, 8 and 15 of a 28 day treatment Cycle. Treatment Cycles were continued until disease progression, unacceptable toxicity, or other discontinuation criteria met.

Arm type	Experimental
Investigational medicinal product name	BAL101553
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

BAL101553 30 mg/m² intravenously over 2 hours on Days 1, 8 and 15 of each 28-day treatment cycle.

Arm title	BAL101553: 45 mg/m²

Arm description:

BAL101553 was administered at 45 mg/m² as an IV infusion over 2 hours on Days 1, 8 and 15 of a 28 day treatment Cycle. Treatment Cycles were continued until disease progression, unacceptable toxicity, or other discontinuation criteria met.

Arm type	Experimental

Investigational medicinal product name	BAL101553
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

BAL101553 45 mg/m² intravenously over 2 hours on Days 1, 8 and 15 of each 28-day treatment cycle.

Arm title	BAL101553: 60 mg/m²

Arm description:

BAL101553 was administered at 60 mg/m² as an IV infusion over 2 hours on Days 1, 8 and 15 of a 28 day treatment Cycle. Treatment Cycles were continued until disease progression, unacceptable toxicity, or other discontinuation criteria met.

Arm type	Experimental
Investigational medicinal product name	BAL101553
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

BAL101553 60 mg/m² intravenously over 2 hours on Days 1, 8 and 15 of each 28-day treatment cycle.

Arm title	BAL101553: 80 mg/m²

Arm description:

BAL101553 was administered at 80 mg/m² as an IV infusion over 2 hours on Days 1, 8 and 15 of a 28 day treatment Cycle. Treatment Cycles were continued until disease progression, unacceptable toxicity, or other discontinuation criteria met.

Arm type	Experimental
Investigational medicinal product name	BAL101553
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

BAL101553 80 mg/m² intravenously over 2 hours on Days 1, 8 and 15 of each 28-day treatment cycle.

Number of subjects in period 1	BAL101553: 15 mg/m²	BAL101553: 30 mg/m²	BAL101553: 45 mg/m²
Started	1	36	8
Completed	0	0	0
Not completed	1	36	8
Consent withdrawn by subject	-	1	-
Disease progression	1	30	7
Death	-	1	-
Admin/ other	-	1	-
AE, intercurrent illness	-	2	1
Protocol deviation	-	1	-

Number of subjects in period 1	BAL101553: 60 mg/m²	BAL101553: 80 mg/m²

Started	21	7
Completed	0	0
Not completed	21	7
Consent withdrawn by subject	1	2
Disease progression	18	3
Death	-	-
Admin/ other	-	-
AE, intercurrent illness	2	2
Protocol deviation	-	-

Baseline characteristics

Reporting groups	
Reporting group title	BAL101553: 15 mg/m²
Reporting group description:	
BAL101553 was administered at 15 mg/m² as an IV infusion over 2 hours on Days 1, 8 and 15 of a 28 day treatment Cycle. Treatment Cycles were continued until disease progression, unacceptable toxicity, or other discontinuation criteria met.	
Reporting group title	BAL101553: 30 mg/m²
Reporting group description:	
BAL101553 was administered at 30 mg/m² as an IV infusion over 2 hours on Days 1, 8 and 15 of a 28 day treatment Cycle. Treatment Cycles were continued until disease progression, unacceptable toxicity, or other discontinuation criteria met.	
Reporting group title	BAL101553: 45 mg/m²
Reporting group description:	
BAL101553 was administered at 45 mg/m² as an IV infusion over 2 hours on Days 1, 8 and 15 of a 28 day treatment Cycle. Treatment Cycles were continued until disease progression, unacceptable toxicity, or other discontinuation criteria met.	
Reporting group title	BAL101553: 60 mg/m²
Reporting group description:	
BAL101553 was administered at 60 mg/m² as an IV infusion over 2 hours on Days 1, 8 and 15 of a 28 day treatment Cycle. Treatment Cycles were continued until disease progression, unacceptable toxicity, or other discontinuation criteria met.	
Reporting group title	BAL101553: 80 mg/m²
Reporting group description:	
BAL101553 was administered at 80 mg/m² as an IV infusion over 2 hours on Days 1, 8 and 15 of a 28 day treatment Cycle. Treatment Cycles were continued until disease progression, unacceptable toxicity, or other discontinuation criteria met.	

Reporting group values	BAL101553: 15 mg/m²	BAL101553: 30 mg/m²	BAL101553: 45 mg/m²
Number of subjects	1	36	8
Age categorical			
Units: Subjects			
Adults (18-64 years)	1	26	2
From 65-84 years	0	10	6
Age continuous			
Units: years			
median	51	60	67
full range (min-max)	51 to 51	32 to 79	47 to 76
Gender categorical			
Units: Subjects			
Female	1	16	3
Male	0	20	5

Reporting group values	BAL101553: 60 mg/m²	BAL101553: 80 mg/m²	Total
Number of subjects	21	7	73
Age categorical			
Units: Subjects			
Adults (18-64 years)	16	5	50
From 65-84 years	5	2	23

Age continuous Units: years			
median	57	55	
full range (min-max)	29 to 80	45 to 70	-
Gender categorical Units: Subjects			
Female	11	3	34
Male	10	4	39

End points

End points reporting groups

Reporting group title	BAL101553: 15 mg/m²
Reporting group description:	
BAL101553 was administered at 15 mg/m² as an IV infusion over 2 hours on Days 1, 8 and 15 of a 28 day treatment Cycle. Treatment Cycles were continued until disease progression, unacceptable toxicity, or other discontinuation criteria met.	
Reporting group title	BAL101553: 30 mg/m²
Reporting group description:	
BAL101553 was administered at 30 mg/m² as an IV infusion over 2 hours on Days 1, 8 and 15 of a 28 day treatment Cycle. Treatment Cycles were continued until disease progression, unacceptable toxicity, or other discontinuation criteria met.	
Reporting group title	BAL101553: 45 mg/m²
Reporting group description:	
BAL101553 was administered at 45 mg/m² as an IV infusion over 2 hours on Days 1, 8 and 15 of a 28 day treatment Cycle. Treatment Cycles were continued until disease progression, unacceptable toxicity, or other discontinuation criteria met.	
Reporting group title	BAL101553: 60 mg/m²
Reporting group description:	
BAL101553 was administered at 60 mg/m² as an IV infusion over 2 hours on Days 1, 8 and 15 of a 28 day treatment Cycle. Treatment Cycles were continued until disease progression, unacceptable toxicity, or other discontinuation criteria met.	
Reporting group title	BAL101553: 80 mg/m²
Reporting group description:	
BAL101553 was administered at 80 mg/m² as an IV infusion over 2 hours on Days 1, 8 and 15 of a 28 day treatment Cycle. Treatment Cycles were continued until disease progression, unacceptable toxicity, or other discontinuation criteria met.	

Primary: Maximum tolerated dose (MTD)

End point title	Maximum tolerated dose (MTD)[1]
End point description:	
MTD: highest dose level of BAL101553 at which no more than 1 of 6 MTD-evaluable subjects experienced dose limiting toxicities (DLT). DLT: an adverse event or abnormal laboratory value as defined in the protocol that is related to BAL101553. MTD-evaluable subjects: Phase 1 subjects who received at least one dose of BAL101553 and experienced a DLT, or patients who received all three doses of BAL101553 in Cycle 1 without a DLT.	
End point type	Primary
End point timeframe:	
Cycle 1 (28 days)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	BAL101553: 15 mg/m²	BAL101553: 30 mg/m²	BAL101553: 45 mg/m²	BAL101553: 60 mg/m²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	3	3	6
Units: Subjects with DLTs	0	0	0	1

End point values	BAL101553: 80 mg/m²			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Subjects with DLTs	2			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: AUC of BAL101553 and BAL27862 (the active metabolite)

End point title	PK Parameter: AUC of BAL101553 and BAL27862 (the active metabolite)

End point description:

Area under the plasma concentration time curve from time point zero to infinity

End point type	Secondary

End point timeframe:

Day 1 of Cycle 1

End point values	BAL101553: 15 mg/m²	BAL101553: 30 mg/m²	BAL101553: 45 mg/m²	BAL101553: 60 mg/m²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	36	8	21
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
BAL101553	917 (± 0)	2520 (± 44.0)	2340 (± 257)	3440 (± 47.8)
BAL27862	2110 (± 0)	3620 (± 55.7)	5090 (± 62.9)	7180 (± 44.5)

End point values	BAL101553: 80 mg/m²			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
BAL101553	5640 (± 36.5)			
BAL27862	7950 (± 40.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Cmax of BAL101553 and BAL27862 (the active metabolite)

End point title	PK Parameter: Cmax of BAL101553 and BAL27862 (the active metabolite)

End point description:

Maximum drug concentration observed in plasma

End point type	Secondary

End point timeframe:

Day 1 of Cycle 1

End point values	BAL101553: 15 mg/m²	BAL101553: 30 mg/m²	BAL101553: 45 mg/m²	BAL101553: 60 mg/m²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	36	8	21
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
BAL101553	556 (± 0)	1060 (± 51.7)	1130 (± 350)	1320 (± 137)
BAL27862	154 (± 0)	267 (± 19.8)	346 (± 26.3)	484 (± 25.1)

End point values	BAL101553: 80 mg/m²			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
BAL101553	3250 (± 24.8)			
BAL27862	601 (± 13.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Tmax of BAL101553 and BAL27862 (the active metabolite)

End point title	PK Parameter: Tmax of BAL101553 and BAL27862 (the active metabolite)

End point description:

Time to maximum plasma concentration

End point type	Secondary

End point timeframe:

Day 1 of Cycle 1

End point values	BAL101553: 15 mg/m²	BAL101553: 30 mg/m²	BAL101553: 45 mg/m²	BAL101553: 60 mg/m²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	36	8	21
Units: hours				
geometric mean (geometric coefficient of variation)				
BAL101553	1.05 (± 0)	1.94 (± 15.9)	1.80 (± 39.6)	1.75 (± 36.9)
BAL27862	2.50 (± 0)	2.13 (± 16.7)	2.30 (± 28.8)	2.34 (± 23.8)

End point values	BAL101553: 80 mg/m²			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: hours				
geometric mean (geometric coefficient of variation)				
BAL101553	1.54 (± 32.9)			
BAL27862	2.33 (± 14.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Terminal half-life of BAL101553 and BAL27862 (the active metabolite)

End point title	PK Parameter: Terminal half-life of BAL101553 and BAL27862 (the active metabolite)

End point description:

End point type	Secondary

End point timeframe:

Day 1 of Cycle 1

End point values	BAL101553: 15 mg/m²	BAL101553: 30 mg/m²	BAL101553: 45 mg/m²	BAL101553: 60 mg/m²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	36	8	21
Units: hours				
geometric mean (geometric coefficient of variation)				
BAL101553	0.908 (± 0)	1.96 (± 44.1)	1.54 (± 20.7)	1.51 (± 33.1)
BAL27862	18.1 (± 0)	12.6 (± 57.2)	12.5 (± 47.7)	13.8 (± 26.5)

End point values	BAL101553: 80 mg/m²			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: hours				
geometric mean (geometric coefficient of variation)				
BAL101553	1.49 (± 15.2)			
BAL27862	12.5 (± 26.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Best overall response in EEP

End point title	Best overall response in EEP

End point description:

The best overall response is the best response recorded from the start of the treatment until disease progression.
Efficacy evaluable population (EEP): all patients who completed Cycle 1 dosing and who underwent at least one on-study clinical tumor assessment or a radiological assessment by RECIST v1.1.

End point type	Secondary

End point timeframe:

Assessed every 8 weeks from time of first dose until disease progression.

End point values	BAL101553: 15 mg/m²	BAL101553: 30 mg/m²	BAL101553: 45 mg/m²	BAL101553: 60 mg/m²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	31	7	15
Units: Number of subjects				
Complete response	0	0	0	0
Partial response	0	1	0	0
Stable disease	1	5	3	5
Progressive disease	0	25	4	10

End point values	BAL101553: 80 mg/m²			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Number of subjects				
Complete response	0			
Partial response	0			
Stable disease	0			
Progressive disease	3			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first administration of BAL101553 up to 28 days after the last administration.	
Adverse event reporting additional description:	
Treatment-emergent adverse events and serious adverse events	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17

Reporting groups	
Reporting group title	BAL101553: 15 mg/m²
Reporting group description:	
BAL101553 was administered at 15 mg/m² as an IV infusion over 2 hours on Days 1, 8 and 15 of a 28 day treatment Cycle. Treatment Cycles were continued until disease progression, unacceptable toxicity, or other discontinuation criteria met.	
Reporting group title	BAL101553: 30 mg/m²
Reporting group description:	
BAL101553 was administered at 30 mg/m² as an IV infusion over 2 hours on Days 1, 8 and 15 of a 28 day treatment Cycle. Treatment Cycles were continued until disease progression, unacceptable toxicity, or other discontinuation criteria met.	
Reporting group title	BAL101553: 45 mg/m²
Reporting group description:	
BAL101553 was administered at 45 mg/m² as an IV infusion over 2 hours on Days 1, 8 and 15 of a 28 day treatment Cycle. Treatment Cycles were continued until disease progression, unacceptable toxicity, or other discontinuation criteria met.	
Reporting group title	BAL101553: 60 mg/m²
Reporting group description:	
BAL101553 was administered at 60 mg/m² as an IV infusion over 2 hours on Days 1, 8 and 15 of a 28 day treatment Cycle. Treatment Cycles were continued until disease progression, unacceptable toxicity, or other discontinuation criteria met.	
Reporting group title	BAL101553: 80 mg/m²
Reporting group description:	
BAL101553 was administered at 80 mg/m² as an IV infusion over 2 hours on Days 1, 8 and 15 of a 28 day treatment Cycle. Treatment Cycles were continued until disease progression, unacceptable toxicity, or other discontinuation criteria met.	

Serious adverse events	BAL101553: 15 mg/m²	BAL101553: 30 mg/m²	BAL101553: 45 mg/m²
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	14 / 36 (38.89%)	3 / 8 (37.50%)
number of deaths (all causes)	0	2	1
number of deaths resulting from adverse events	0	2	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			

subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (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
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (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
Hypotension			
subjects affected / exposed	0 / 1 (0.00%)	1 / 36 (2.78%)	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
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	0 / 1 (0.00%)	1 / 36 (2.78%)	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 / 1	0 / 0
Gait disturbance			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (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
General physical health deterioration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (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
Pyrexia			
subjects affected / exposed	0 / 1 (0.00%)	2 / 36 (5.56%)	0 / 8 (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
Respiratory, thoracic and mediastinal disorders			
Bronchial obstruction			

subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (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 / 1
Pleuritic pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 36 (2.78%)	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
Pulmonary embolism			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (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
Investigations			
Electrocardiogram T wave inversion			
subjects affected / exposed	0 / 1 (0.00%)	1 / 36 (2.78%)	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
Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	0 / 1 (0.00%)	1 / 36 (2.78%)	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
Incorrect drug administration rate			
subjects affected / exposed	0 / 1 (0.00%)	1 / 36 (2.78%)	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
Radiation pneumonitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (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 / 1 (0.00%)	0 / 36 (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

Myocardial infarction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (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
Myocarditis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (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
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (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
Myasthenia gravis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (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
Syncope			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (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 / 1 (0.00%)	0 / 36 (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
Abdominal pain upper			

subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (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
Acute abdomen			
subjects affected / exposed	0 / 1 (0.00%)	1 / 36 (2.78%)	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 / 1	0 / 0
Ascites			
subjects affected / exposed	0 / 1 (0.00%)	1 / 36 (2.78%)	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
Constipation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (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
Diarrhoea			
subjects affected / exposed	0 / 1 (0.00%)	1 / 36 (2.78%)	0 / 8 (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
Intestinal obstruction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (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
Large intestinal obstruction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (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
Melaena			
subjects affected / exposed	0 / 1 (0.00%)	1 / 36 (2.78%)	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
Nausea			

subjects affected / exposed	0 / 1 (0.00%)	1 / 36 (2.78%)	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
Small intestinal obstruction			
subjects affected / exposed	0 / 1 (0.00%)	1 / 36 (2.78%)	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
Vomiting			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (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			
Bile duct obstruction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (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
Cholangitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 36 (2.78%)	0 / 8 (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
Jaundice			
subjects affected / exposed	0 / 1 (0.00%)	1 / 36 (2.78%)	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
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (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
Musculoskeletal and connective tissue disorders			
Mobility decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (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

Infections and infestations			
Biliary sepsis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 36 (2.78%)	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
Device related infection			
subjects affected / exposed	0 / 1 (0.00%)	1 / 36 (2.78%)	0 / 8 (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
Sepsis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 36 (2.78%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (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 / 1 (0.00%)	1 / 36 (2.78%)	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

Serious adverse events	BAL101553: 60 mg/m²	BAL101553: 80 mg/m²	
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 21 (66.67%)	5 / 7 (71.43%)	
number of deaths (all causes)	2	0	
number of deaths resulting from adverse events	2	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	2 / 21 (9.52%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			

subjects affected / exposed	2 / 21 (9.52%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	2 / 21 (9.52%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gait disturbance			
subjects affected / exposed	0 / 21 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 21 (4.76%)	2 / 7 (28.57%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchial obstruction			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleuritic pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pulmonary embolism			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Electrocardiogram T wave inversion			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incorrect drug administration rate			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiation pneumonitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocarditis			

subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myasthenia gravis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 21 (9.52%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute abdomen			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ascites			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 21 (4.76%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	1 / 21 (4.76%)	2 / 7 (28.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct obstruction			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Mobility decreased			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Biliary sepsis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			

subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	BAL101553: 15 mg/m²	BAL101553: 30 mg/m²	BAL101553: 45 mg/m²
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	35 / 36 (97.22%)	8 / 8 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	2
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypertension			

subjects affected / exposed	1 / 1 (100.00%)	6 / 36 (16.67%)	3 / 8 (37.50%)
occurrences (all)	1	18	7
Hypotension			
subjects affected / exposed	0 / 1 (0.00%)	2 / 36 (5.56%)	2 / 8 (25.00%)
occurrences (all)	0	2	3
Thrombophlebitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Chills			
subjects affected / exposed	1 / 1 (100.00%)	2 / 36 (5.56%)	0 / 8 (0.00%)
occurrences (all)	1	2	0
Fatigue			
subjects affected / exposed	0 / 1 (0.00%)	13 / 36 (36.11%)	4 / 8 (50.00%)
occurrences (all)	0	15	6
Gait disturbance			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Infusion site erythema			
subjects affected / exposed	0 / 1 (0.00%)	1 / 36 (2.78%)	2 / 8 (25.00%)
occurrences (all)	0	1	3
Infusion site pruritus			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Infusion site reaction			
subjects affected / exposed	1 / 1 (100.00%)	4 / 36 (11.11%)	0 / 8 (0.00%)
occurrences (all)	2	10	0
Infusion site thrombosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Mucosal inflammation			
subjects affected / exposed	0 / 1 (0.00%)	2 / 36 (5.56%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Non-cardiac chest pain			

subjects affected / exposed	0 / 1 (0.00%)	2 / 36 (5.56%)	0 / 8 (0.00%)
occurrences (all)	0	3	0
Oedema peripheral			
subjects affected / exposed	0 / 1 (0.00%)	1 / 36 (2.78%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Puncture site erythema			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Puncture site pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 1 (0.00%)	2 / 36 (5.56%)	1 / 8 (12.50%)
occurrences (all)	0	2	2
Reproductive system and breast disorders			
Genital swelling			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 1 (0.00%)	3 / 36 (8.33%)	0 / 8 (0.00%)
occurrences (all)	0	3	0
Dyspnoea			
subjects affected / exposed	0 / 1 (0.00%)	4 / 36 (11.11%)	3 / 8 (37.50%)
occurrences (all)	0	4	4
Dyspnoea exertional			
subjects affected / exposed	1 / 1 (100.00%)	2 / 36 (5.56%)	0 / 8 (0.00%)
occurrences (all)	1	3	0
Haemoptysis			
subjects affected / exposed	0 / 1 (0.00%)	2 / 36 (5.56%)	1 / 8 (12.50%)
occurrences (all)	0	2	1
Hiccups			
subjects affected / exposed	0 / 1 (0.00%)	2 / 36 (5.56%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Tachypnoea			

subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 1 (0.00%)	3 / 36 (8.33%)	0 / 8 (0.00%)
occurrences (all)	0	3	0
Depressed mood			
subjects affected / exposed	1 / 1 (100.00%)	1 / 36 (2.78%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Insomnia			
subjects affected / exposed	1 / 1 (100.00%)	3 / 36 (8.33%)	0 / 8 (0.00%)
occurrences (all)	2	3	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	6 / 36 (16.67%)	0 / 8 (0.00%)
occurrences (all)	0	7	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	4 / 36 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	6	0
Blood albumin decreased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 36 (2.78%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 1 (0.00%)	3 / 36 (8.33%)	0 / 8 (0.00%)
occurrences (all)	0	4	0
Blood creatinine increased			
subjects affected / exposed	1 / 1 (100.00%)	1 / 36 (2.78%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Cells in urine			
subjects affected / exposed	1 / 1 (100.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 1 (100.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
QRS axis abnormal			

subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	0 / 1 (0.00%)	4 / 36 (11.11%)	1 / 8 (12.50%)
occurrences (all)	0	4	1
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 1 (0.00%)	2 / 36 (5.56%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 1 (0.00%)	2 / 36 (5.56%)	0 / 8 (0.00%)
occurrences (all)	0	3	0
Sinus tachycardia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 1 (0.00%)	1 / 36 (2.78%)	0 / 8 (0.00%)
occurrences (all)	0	3	0
Dysgeusia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 1 (100.00%)	4 / 36 (11.11%)	1 / 8 (12.50%)
occurrences (all)	1	5	1
Lethargy			

subjects affected / exposed	0 / 1 (0.00%)	4 / 36 (11.11%)	1 / 8 (12.50%)
occurrences (all)	0	4	1
Memory impairment			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 1 (0.00%)	2 / 36 (5.56%)	3 / 8 (37.50%)
occurrences (all)	0	2	3
Nystagmus			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	1 / 1 (100.00%)	1 / 36 (2.78%)	1 / 8 (12.50%)
occurrences (all)	1	1	1
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 1 (0.00%)	1 / 36 (2.78%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 1 (0.00%)	9 / 36 (25.00%)	2 / 8 (25.00%)
occurrences (all)	0	9	3
Leukocytosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 1 (0.00%)	3 / 36 (8.33%)	0 / 8 (0.00%)
occurrences (all)	0	3	0
Abdominal distension			
subjects affected / exposed	0 / 1 (0.00%)	1 / 36 (2.78%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			

subjects affected / exposed	1 / 1 (100.00%)	3 / 36 (8.33%)	0 / 8 (0.00%)
occurrences (all)	1	3	0
Abdominal pain lower			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 1 (0.00%)	4 / 36 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	5	0
Constipation			
subjects affected / exposed	0 / 1 (0.00%)	10 / 36 (27.78%)	1 / 8 (12.50%)
occurrences (all)	0	12	1
Diarrhoea			
subjects affected / exposed	1 / 1 (100.00%)	10 / 36 (27.78%)	4 / 8 (50.00%)
occurrences (all)	1	14	4
Dry mouth			
subjects affected / exposed	0 / 1 (0.00%)	2 / 36 (5.56%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 1 (0.00%)	1 / 36 (2.78%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Nausea			
subjects affected / exposed	1 / 1 (100.00%)	12 / 36 (33.33%)	4 / 8 (50.00%)
occurrences (all)	2	18	6
Oesophageal haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Rectal haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 1 (100.00%)	7 / 36 (19.44%)	2 / 8 (25.00%)
occurrences (all)	2	10	4
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	1 / 1 (100.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	0 / 1 (0.00%)	4 / 36 (11.11%)	1 / 8 (12.50%)
occurrences (all)	0	4	1
Rash			
subjects affected / exposed	1 / 1 (100.00%)	5 / 36 (13.89%)	0 / 8 (0.00%)
occurrences (all)	1	5	0
Rash macular			
subjects affected / exposed	0 / 1 (0.00%)	2 / 36 (5.56%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Rash papular			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Skin reaction			
subjects affected / exposed	1 / 1 (100.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 1 (100.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Urinary hesitation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 1 (0.00%)	4 / 36 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	5	0
Back pain			
subjects affected / exposed	0 / 1 (0.00%)	8 / 36 (22.22%)	0 / 8 (0.00%)
occurrences (all)	0	11	0
Flank pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			

subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Muscle tightness			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 1 (0.00%)	1 / 36 (2.78%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 1 (0.00%)	2 / 36 (5.56%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal pain			
subjects affected / exposed	0 / 1 (0.00%)	4 / 36 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	4	0
Myalgia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 1 (0.00%)	2 / 36 (5.56%)	1 / 8 (12.50%)
occurrences (all)	0	2	1
Pain in jaw			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	0 / 1 (0.00%)	2 / 36 (5.56%)	0 / 8 (0.00%)
occurrences (all)	0	3	0
Oral candidiasis			
subjects affected / exposed	0 / 1 (0.00%)	3 / 36 (8.33%)	0 / 8 (0.00%)
occurrences (all)	0	4	0
Paronychia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1

Upper respiratory tract infection			
subjects affected / exposed	0 / 1 (0.00%)	4 / 36 (11.11%)	1 / 8 (12.50%)
occurrences (all)	0	4	1
Urinary tract infection			
subjects affected / exposed	1 / 1 (100.00%)	2 / 36 (5.56%)	0 / 8 (0.00%)
occurrences (all)	2	3	0
Urinary tract infection bacterial			
subjects affected / exposed	0 / 1 (0.00%)	0 / 36 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 1 (100.00%)	11 / 36 (30.56%)	1 / 8 (12.50%)
occurrences (all)	1	13	1
Diabetes mellitus			
subjects affected / exposed	0 / 1 (0.00%)	2 / 36 (5.56%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Hypercalcaemia			
subjects affected / exposed	1 / 1 (100.00%)	1 / 36 (2.78%)	1 / 8 (12.50%)
occurrences (all)	1	1	1
Hyperglycaemia			
subjects affected / exposed	0 / 1 (0.00%)	4 / 36 (11.11%)	1 / 8 (12.50%)
occurrences (all)	0	4	1
Hypokalaemia			
subjects affected / exposed	0 / 1 (0.00%)	2 / 36 (5.56%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Hyponatraemia			
subjects affected / exposed	0 / 1 (0.00%)	2 / 36 (5.56%)	1 / 8 (12.50%)
occurrences (all)	0	2	1

Non-serious adverse events	BAL101553: 60 mg/m²	BAL101553: 80 mg/m²	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 21 (100.00%)	7 / 7 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences (all)	2	0	

Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 21 (4.76%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Flushing			
subjects affected / exposed	0 / 21 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	12 / 21 (57.14%)	6 / 7 (85.71%)	
occurrences (all)	30	10	
Hypotension			
subjects affected / exposed	0 / 21 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Thrombophlebitis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	3 / 21 (14.29%)	1 / 7 (14.29%)	
occurrences (all)	5	2	
Fatigue			
subjects affected / exposed	12 / 21 (57.14%)	4 / 7 (57.14%)	
occurrences (all)	17	4	
Gait disturbance			
subjects affected / exposed	1 / 21 (4.76%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Infusion site erythema			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Infusion site pruritus			
subjects affected / exposed	1 / 21 (4.76%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Infusion site reaction			
subjects affected / exposed	2 / 21 (9.52%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Infusion site thrombosis			

subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Mucosal inflammation			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 21 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Oedema peripheral			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Puncture site erythema			
subjects affected / exposed	0 / 21 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Puncture site pain			
subjects affected / exposed	0 / 21 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	7 / 21 (33.33%)	1 / 7 (14.29%)	
occurrences (all)	7	3	
Reproductive system and breast disorders			
Genital swelling			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 21 (4.76%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Dyspnoea			
subjects affected / exposed	3 / 21 (14.29%)	2 / 7 (28.57%)	
occurrences (all)	4	2	
Dyspnoea exertional			
subjects affected / exposed	2 / 21 (9.52%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Haemoptysis			

subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Hiccups			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Tachypnoea			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 21 (19.05%)	1 / 7 (14.29%)	
occurrences (all)	4	1	
Depressed mood			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Insomnia			
subjects affected / exposed	4 / 21 (19.05%)	0 / 7 (0.00%)	
occurrences (all)	4	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Blood albumin decreased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Blood creatinine increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Cells in urine			

subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Lymphocyte count decreased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
QRS axis abnormal			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Weight decreased			
subjects affected / exposed	1 / 21 (4.76%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 21 (9.52%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 21 (4.76%)	2 / 7 (28.57%)	
occurrences (all)	1	3	
Palpitations			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Sinus tachycardia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Tachycardia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Ataxia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Dizziness			
subjects affected / exposed	2 / 21 (9.52%)	2 / 7 (28.57%)	
occurrences (all)	3	2	
Dysgeusia			

subjects affected / exposed	4 / 21 (19.05%)	1 / 7 (14.29%)	
occurrences (all)	4	1	
Headache			
subjects affected / exposed	6 / 21 (28.57%)	2 / 7 (28.57%)	
occurrences (all)	14	2	
Lethargy			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Memory impairment			
subjects affected / exposed	0 / 21 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Migraine			
subjects affected / exposed	0 / 21 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	
Neuropathy peripheral			
subjects affected / exposed	3 / 21 (14.29%)	5 / 7 (71.43%)	
occurrences (all)	5	6	
Nystagmus			
subjects affected / exposed	0 / 21 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Paraesthesia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Peripheral sensory neuropathy			
subjects affected / exposed	2 / 21 (9.52%)	1 / 7 (14.29%)	
occurrences (all)	2	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 21 (19.05%)	0 / 7 (0.00%)	
occurrences (all)	6	0	
Leukocytosis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal discomfort			

subjects affected / exposed	2 / 21 (9.52%)	1 / 7 (14.29%)	
occurrences (all)	2	2	
Abdominal distension			
subjects affected / exposed	1 / 21 (4.76%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Abdominal pain			
subjects affected / exposed	6 / 21 (28.57%)	1 / 7 (14.29%)	
occurrences (all)	8	5	
Abdominal pain lower			
subjects affected / exposed	2 / 21 (9.52%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Abdominal pain upper			
subjects affected / exposed	3 / 21 (14.29%)	1 / 7 (14.29%)	
occurrences (all)	6	1	
Constipation			
subjects affected / exposed	11 / 21 (52.38%)	3 / 7 (42.86%)	
occurrences (all)	14	3	
Diarrhoea			
subjects affected / exposed	13 / 21 (61.90%)	4 / 7 (57.14%)	
occurrences (all)	22	6	
Dry mouth			
subjects affected / exposed	2 / 21 (9.52%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 21 (9.52%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Nausea			
subjects affected / exposed	14 / 21 (66.67%)	7 / 7 (100.00%)	
occurrences (all)	31	12	
Oesophageal haemorrhage			
subjects affected / exposed	0 / 21 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Proctalgia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Rectal haemorrhage			

subjects affected / exposed	2 / 21 (9.52%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Vomiting			
subjects affected / exposed	13 / 21 (61.90%)	7 / 7 (100.00%)	
occurrences (all)	22	12	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Rash			
subjects affected / exposed	2 / 21 (9.52%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Rash macular			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Rash papular			
subjects affected / exposed	2 / 21 (9.52%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Skin reaction			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Urinary hesitation			
subjects affected / exposed	0 / 21 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Back pain			

subjects affected / exposed	7 / 21 (33.33%)	2 / 7 (28.57%)	
occurrences (all)	10	3	
Flank pain			
subjects affected / exposed	2 / 21 (9.52%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Muscle spasms			
subjects affected / exposed	2 / 21 (9.52%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Muscle tightness			
subjects affected / exposed	0 / 21 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Muscular weakness			
subjects affected / exposed	0 / 21 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 21 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Musculoskeletal pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Neck pain			
subjects affected / exposed	2 / 21 (9.52%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Pain in extremity			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Pain in jaw			
subjects affected / exposed	0 / 21 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	0 / 21 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	

Oral candidiasis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Paronychia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	3 / 21 (14.29%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Urinary tract infection bacterial			
subjects affected / exposed	0 / 21 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	11 / 21 (52.38%)	3 / 7 (42.86%)	
occurrences (all)	13	3	
Diabetes mellitus			
subjects affected / exposed	0 / 21 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Hypercalcaemia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Hyperglycaemia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Hypokalaemia			
subjects affected / exposed	3 / 21 (14.29%)	0 / 7 (0.00%)	
occurrences (all)	5	0	
Hyponatraemia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 7 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 January 2012	Change of the infusion carrier solution to Ringer Lactate and addition of optional pre- and post-dose and/or parallel-infusion with Ringer Lactate or physiologic saline.
18 July 2012	Exclusion of patients with uncontrolled baseline hypertension or with history of cerebral hemorrhage, cerebral aneurysm, ischemic stroke or transient ischemic attack. Increased frequency of BP, ECG, and cardiac troponin assessments.
12 May 2014	Definition of Phase 2a design: inclusion of 40 evaluable patients with specific tumor types; randomization (1:1) to 60 mg/m² or 30 mg/m²; introduction of optional functional imaging.
11 May 2015	Definition of patient number per tumor type; changed definition of the Efficacy Evaluable Population (EEP); changed patient replacement criteria.
02 June 2015	Randomization to 30 mg/m² or 45 mg/m² instead of 60 mg/m² because of cardiac safety concerns at 60 mg/m². Introduction of additional troponin and ECG assessments.
27 November 2015	Clarification of EEP definition, patient replacement criteria, and treatment of missing RECIST data.
02 December 2015	Treatment of all patients at 30 mg/m² following observation of myocardial injury in one patient at 45 mg/m².

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported