Clinical trial results:
Phase 1, Open Label, Multiple Dose Escalation Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of CP-751,871 in Patients with Advanced Solid Tumours

Summary

EudraCT number	2005-001224-36
Trial protocol	GB
Global end of trial date	26 October 2012

Results information

Result version number	v1
This version publication date	16 March 2016
First version publication date	02 August 2015
Summary attachment (see zip file)	A4021010 EU Posting (A4021010.pdf)

Trial information

Trial identification

Sponsor protocol code	A4021010

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00474760
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001800 718-1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001800 718-1021, ClinicalTrials.gov_Inquiries@pfizer.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	04 May 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 October 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To define the safety, tolerability, maximum tolerated dose (MTD) and recommended Phase 2 dose (RP2D) of CP-751,871 in patients with advanced solid tumors.

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of trial subjects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 2005
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: 27
Country: Number of subjects enrolled	United States: 38
Worldwide total number of subjects	65
EEA total number of subjects	27

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)	5
Adults (18-64 years)	57
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A Total 65 subjects from two countries received the study drug. The duration of the study was 01 August 2005 to 26 October 2012 and no enrollments were made after 03 September 2008 .

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Figitumumab 3 mg/kg

Arm description:

Figitumumab 3 milligram per kilogram (mg/kg) administered as an intravenous (IV) infusion on Day 1 of each cycle for dose escalation cohort.

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

Dosage and administration details:

Figitumumab 3 mg/kg was supplied as a liquid solution administered as an infusion over 2.5 hours (plus or minus 15 minutes) on Day 1 of each cycle (3 weeks in duration).

Arm title	Figitumumab 6 mg/kg

Arm description:

Figitumumab 6 mg/kg administered as an IV infusion on Day 1 of each cycle (3 weeks in duration) for dose escalation cohort.

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

Dosage and administration details:

Figitumumab 6 mg/kg was supplied as a liquid solution administered as an infusion over 2.5 hours (plus or minus 15 minutes) on Day 1 of each cycle (3 weeks in duration).

Arm title	Figitumumab 10 mg/kg

Arm description:

Figitumumab 10 mg/kg was supplied as a liquid solution administered as an IV infusion on Day 1 of each cycle (3 weeks in duration) for dose escalation cohort.

Arm type	Experimental

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

Dosage and administration details:

Figitumumab 10 mg/kg was supplied as a liquid solution administered as an infusion over 2.5 hours (plus or minus 15 minutes) on Day 1 of each cycle (3 weeks in duration).

Arm title	Figitumumab 20 mg/kg

Arm description:

Figitumumab 20 mg/kg was supplied as a liquid solution administered as an IV infusion on Day 1 of each cycle (3 weeks in duration) for dose escalation cohort.

Arm type	Experimental
Investigational medicinal product name	Figitumumab
Investigational medicinal product code	CP- 751,871
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Figitumumab 20 mg/kg was supplied as a liquid solution administered as an infusion over 2.5 hours (plus or minus 15 minutes) on Day 1 of each cycle (3 weeks in duration).

Arm title	Figitumumab 20 mg/kg RP2D

Arm description:

Figitumumab 20 mg/kg was supplied as a liquid solution administered as an IV infusion on Day 1 of each cycle (3 weeks in duration) for recommended Phase 2 dose [RP2D] extension cohort.

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

Dosage and administration details:

Figitumumab 20 mg/kg was supplied as a liquid solution administered as an infusion over 2.5 hours (plus or minus 15 minutes) on Day 1 of each cycle (3 weeks in duration).

Arm title	Figitumumab 20 mg/kg RP2D ACC+Sarcoma

Arm description:

Figitumumab 20 mg/kg was supplied as a liquid solution administered as an IV infusion on Day 1 of each cycle (3 weeks in duration) for RP2D adrenocortical carcinoma [ACC] and sarcoma extension cohort.

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

Dosage and administration details:

Figitumumab 20 mg/kg was supplied as a liquid solution administered as an infusion over 2.5 hours (plus or minus 15 minutes) on Day 1 of each cycle (3 weeks in duration).

Arm title	Figitumumab 20 mg/kg RP2D ESFT

Arm description:

Figitumumab 20 mg/kg was supplied as a liquid solution administered as an IV infusion on Day 1 of each cycle (4 weeks in duration) for RP2D Ewing’s sarcoma family of tumors [ESFT] extension cohort.

Arm type	Experimental

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

Dosage and administration details:

Figitumumab 20 mg/kg was supplied as a liquid solution administered as an infusion over 2.5 hours (plus or minus 15 minutes) on Day 1 of each cycle (4 weeks in duration).

Number of subjects in period 1	Figitumumab 3 mg/kg	Figitumumab 6 mg/kg	Figitumumab 10 mg/kg
Started	3	3	3
Completed	0	0	0
Not completed	3	3	3
Progressive disease	3	2	3
Adverse Event	-	-	-
Death	-	-	-
Terminated by sponsor	-	-	-
Withdrawal by Subject	-	-	-
Unspecified	-	1	-
Laboratory abnormality	-	-	-

Number of subjects in period 1	Figitumumab 20 mg/kg	Figitumumab 20 mg/kg RP2D	Figitumumab 20 mg/kg RP2D ACC+Sarcoma
Started	3	13	29
Completed	0	1	0
Not completed	3	12	29
Progressive disease	2	8	20
Adverse Event	-	1	7
Death	-	2	-
Terminated by sponsor	-	-	-
Withdrawal by Subject	1	-	1
Unspecified	-	1	-
Laboratory abnormality	-	-	1

Number of subjects in period 1	Figitumumab 20 mg/kg RP2D ESFT
Started	11
Completed	1
Not completed	10
Progressive disease	7
Adverse Event	-
Death	-

Terminated by sponsor	2
Withdrawal by Subject	1
Unspecified	-
Laboratory abnormality	-

Baseline characteristics

Reporting groups	
Reporting group title	Figitumumab 3 mg/kg
Reporting group description:	
Figitumumab 3 milligram per kilogram (mg/kg) administered as an intravenous (IV) infusion on Day 1 of each cycle for dose escalation cohort.	
Reporting group title	Figitumumab 6 mg/kg
Reporting group description:	
Figitumumab 6 mg/kg administered as an IV infusion on Day 1 of each cycle (3 weeks in duration) for dose escalation cohort.	
Reporting group title	Figitumumab 10 mg/kg
Reporting group description:	
Figitumumab 10 mg/kg was supplied as a liquid solution administered as an IV infusion on Day 1 of each cycle (3 weeks in duration) for dose escalation cohort.	
Reporting group title	Figitumumab 20 mg/kg
Reporting group description:	
Figitumumab 20 mg/kg was supplied as a liquid solution administered as an IV infusion on Day 1 of each cycle (3 weeks in duration) for dose escalation cohort.	
Reporting group title	Figitumumab 20 mg/kg RP2D
Reporting group description:	
Figitumumab 20 mg/kg was supplied as a liquid solution administered as an IV infusion on Day 1 of each cycle (3 weeks in duration) for recommended Phase 2 dose [RP2D] extension cohort.	
Reporting group title	Figitumumab 20 mg/kg RP2D ACC+Sarcoma
Reporting group description:	
Figitumumab 20 mg/kg was supplied as a liquid solution administered as an IV infusion on Day 1 of each cycle (3 weeks in duration) for RP2D adrenocortical carcinoma [ACC] and sarcoma extension cohort.	
Reporting group title	Figitumumab 20 mg/kg RP2D ESFT
Reporting group description:	
Figitumumab 20 mg/kg was supplied as a liquid solution administered as an IV infusion on Day 1 of each cycle (4 weeks in duration) for RP2D Ewing’s sarcoma family of tumors [ESFT] extension cohort.	

Reporting group values	Figitumumab 3 mg/kg	Figitumumab 6 mg/kg	Figitumumab 10 mg/kg
Number of subjects	3	3	3
Age categorical Units: Subjects			
Less than (<) 70 years	3	3	3
Equal to or greater than (>=) 70 years	0	0	0
Gender categorical Units: Subjects			
Female	1	2	1
Male	2	1	2

Reporting group values	Figitumumab 20 mg/kg	Figitumumab 20 mg/kg RP2D	Figitumumab 20 mg/kg RP2D ACC+Sarcoma
Number of subjects	3	13	29
Age categorical Units: Subjects			
Less than (<) 70 years	3	13	28

Equal to or greater than (>=) 70 years	0	0	1

Gender categorical Units: Subjects			
Female	0	1	13
Male	3	12	16

Reporting group values	Figitumumab 20 mg/kg RP2D ESFT	Total	
Number of subjects	11	65	
Age categorical Units: Subjects			
Less than (<) 70 years	11	64	
Equal to or greater than (>=) 70 years	0	1	
Gender categorical Units: Subjects			
Female	3	21	
Male	8	44	

End points

End points reporting groups

Reporting group title	Figitumumab 3 mg/kg

Reporting group description:

Figitumumab 3 milligram per kilogram (mg/kg) administered as an intravenous (IV) infusion on Day 1 of each cycle for dose escalation cohort.

Reporting group title	Figitumumab 6 mg/kg

Reporting group description:

Figitumumab 6 mg/kg administered as an IV infusion on Day 1 of each cycle (3 weeks in duration) for dose escalation cohort.

Reporting group title	Figitumumab 10 mg/kg

Reporting group description:

Figitumumab 10 mg/kg was supplied as a liquid solution administered as an IV infusion on Day 1 of each cycle (3 weeks in duration) for dose escalation cohort.

Reporting group title	Figitumumab 20 mg/kg

Reporting group description:

Figitumumab 20 mg/kg was supplied as a liquid solution administered as an IV infusion on Day 1 of each cycle (3 weeks in duration) for dose escalation cohort.

Reporting group title	Figitumumab 20 mg/kg RP2D

Reporting group description:

Figitumumab 20 mg/kg was supplied as a liquid solution administered as an IV infusion on Day 1 of each cycle (3 weeks in duration) for recommended Phase 2 dose [RP2D] extension cohort.

Reporting group title	Figitumumab 20 mg/kg RP2D ACC+Sarcoma

Reporting group description:

Figitumumab 20 mg/kg was supplied as a liquid solution administered as an IV infusion on Day 1 of each cycle (3 weeks in duration) for RP2D adrenocortical carcinoma [ACC] and sarcoma extension cohort.

Reporting group title	Figitumumab 20 mg/kg RP2D ESFT

Reporting group description:

Figitumumab 20 mg/kg was supplied as a liquid solution administered as an IV infusion on Day 1 of each cycle (4 weeks in duration) for RP2D Ewing's sarcoma family of tumors [ESFT] extension cohort.

Subject analysis set title	Figitumumab 20 mg/kg RP2D Every 3 Weeks
Subject analysis set type	Safety analysis

Subject analysis set description:

Figitumumab 20 mg/kg was supplied as a liquid solution administered as an IV infusion over 2.5 hours (plus or minus 15 minutes) on Day 1 of each cycle (3 weeks in duration) for RP2D, and RP2D ACC and sarcoma extension cohorts.

Primary: Number of Subjecs With Treatment-emergent Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Subjecs With Treatment-emergent Adverse Events (AEs) and Serious Adverse Events (SAEs)[1]

End point description:

An AE was any untoward medical occurrence in a subjects who received study drug without regard to possibility of causal relationship. An SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent are events between first dose of study drug and up to 150 days after last dose that were absent before treatment or that worsened relative to pretreatment state. All enrolled subjects who started treatment.

End point type	Primary

End point timeframe:

Baseline up to 150 days after the last administration of study drug

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: Only descriptive data was planned to be reported for this endpoint.

End point values	Figitumumab 3 mg/kg	Figitumumab 6 mg/kg	Figitumumab 10 mg/kg	Figitumumab 20 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: subjects				
AEs	3	3	3	3
SAEs	2	1	3	1

End point values	Figitumumab 20 mg/kg RP2D	Figitumumab 20 mg/kg RP2D ACC+Sarcoma	Figitumumab 20 mg/kg RP2D ESFT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	29	11	
Units: subjects				
AEs	13	29	11	
SAEs	5	17	5	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Dose Limiting Toxicities (DLTs)

End point title	Number of Subjects With Dose Limiting Toxicities (DLTs)[2][3]

End point description:

DLTs were defined as any 1 of the following adverse events (AEs) that occurred in Cycle 1 following treatment with figitumumab and was considered related to the drug: Any National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events version (v) 3.0 (CTCAE) Grade greater than equal to (>=4) treatment-related hematologic AEs (that lasted greater than (>)7 days) and/or required therapy, Any CTCAE Grade >=3 treatment-related non-hematologic AEs despite optimal supportive care, Grade 2 or greater allergic reaction or infusion reaction (required therapy but responded promptly to symptomatic treatment) that affected vital organs and Mitral valve regurgitation > mild. Safety Population

End point type	Primary

End point timeframe:

Baseline up to Day 28 (end of cycle 1)

Notes:

[2] - 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: DLTs was analysed in all subjects.

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: DLTs
was analyzed in subjects of Figitumumab 3 mg/kg , 6 mg/kg , 10 mg/kg , 20 mg/kg , reporting arms onl y.

End point values	Figitumumab 3 mg/kg	Figitumumab 6 mg/kg	Figitumumab 10 mg/kg	Figitumumab 20 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: subjects				
number (not applicable)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) in Cycle 1

End point title	Maximum Observed Plasma Concentration (Cmax) in Cycle 1[4]

End point description:

All subjects treated who had at least 1 of the pharmacokinetic (PK) parameters of primary interest. Summaries for figitumumab 20 mg/kg RP2D, and figitumumab 20 mg/kg RP2D ACC and sarcoma extension cohorts were combined into 1 reporting group: figitumumab 20 mg/kg RP2D every 3 weeks.

End point type	Secondary

End point timeframe:

Cycle 1: 0 (predose), 1, 24 and 72 hours, 7 and 14 days postdose

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cmax in Cycle 1 was analyzed in subjects of Figitumumab 3 mg/kg , 6 mg/kg , 10 mg/kg , 20 mg/kg , 20 mg/kg (RP2D ESFT), 20 mg/kg (RP2D

End point values	Figitumumab 3 mg/kg	Figitumumab 6 mg/kg	Figitumumab 10 mg/kg	Figitumumab 20 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[5]	3[6]	3[7]	3[8]
Units: milligram/liter (mg/L)				
arithmetic mean (standard deviation)	57.77 (± 2.658)	134.7 (± 31.754)	211 (± 59.808)	463 (± 97.964)

Notes:

[5] - N=number of subjects evaluable for the outcome measure.

[6] - N=number of subjects evaluable for the outcome measure.

[7] - N=number of subjects evaluable for the outcome measure.

[8] - N=number of subjects evaluable for the outcome measure.

End point values	Figitumumab 20 mg/kg RP2D ESFT	Figitumumab 20 mg/kg RP2D Every 3 Weeks		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9[9]	34[10]		
Units: milligram/liter (mg/L)				
arithmetic mean (standard deviation)	392 (± 90.308)	457.5 (± 135.68)		

Notes:

[9] - N=number of subjects evaluable for the outcome measure.

[10] - N=number of subjects evaluable for the outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) in Cycle 4

End point title	Maximum Observed Plasma Concentration (Cmax) in Cycle 4[11]

End point description:

All subjects treated who had at least 1 of the PK parameters of primary interest in extension cohorts. Summaries for figitumumab 20 mg/kg RP2D, and figitumumab 20 mg/kg RP2D ACC and sarcoma extension cohorts were combined into 1 reporting group: figitumumab 20 mg/kg RP2D every 3 weeks.

End point type	Secondary

End point timeframe:

Cycle 4: 0 (predose), 1, 24 and 72 hours, 7 and 14 days postdose

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification:
Cmax in Cycle 4 was analyzed in subjects of Figitumumab 3 mg/kg , 6 mg/kg , 10 mg/kg , 20 mg/kg , 2 0 mg/kg (RP2D ESFT), 20 mg/kg (RP2D Every 3 Weeks) reporting arms only

End point values	Figitumumab 20 mg/kg RP2D ESFT	Figitumumab 20 mg/kg RP2D Every 3 Weeks		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	6[12]	16[13]		
Units: mg/L				
arithmetic mean (standard deviation)	650.8 (± 169.92)	697.2 (± 165.4)		

Notes:

[12] - N=number of subjects evaluable for the outcome measure.

[13] - N=number of subjects evaluable for the outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Observed Plasma Concentration (Tmax) in Cycle 1

End point title	Time to Reach Maximum Observed Plasma Concentration (Tmax) in Cycle 1[14]

End point description:

All subjects treated who had at least 1 of the PK parameters of primary interest. Summaries for figitumumab 20 mg/kg RP2D, and figitumumab 20 mg/kg RP2D ACC and sarcoma extension cohorts were combined into 1 reporting group: figitumumab 20 mg/kg RP2D every 3 weeks.

End point type	Secondary

End point timeframe:

Cycle 1: 0 (predose), 1, 24 and 72 hours, 7 and 14 days postdose

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Tmax in cycle 1 was analyzed in subjects of Figitumumab 3 mg/kg , 6 mg/kg , 10 mg/kg , 20 mg/kg , 20 mg/kg (RP2D ESFT), 20 mg/kg (RP2D Every 3 Weeks) reporting arms only.

End point values	Figitumumab 3 mg/kg	Figitumumab 6 mg/kg	Figitumumab 10 mg/kg	Figitumumab 20 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[15]	3[16]	3[17]	3[18]
Units: Hours				
arithmetic mean (standard deviation)	8.361 (± 13.552)	1.147 (± 0.117)	1.043 (± 0.075)	0.678 (± 0.558)

Notes:

[15] - N=number of subjects evaluable for the outcome measure.

[16] - N=number of subjects evaluable for the outcome measure.

[17] - N=number of subjects evaluable for the outcome measure.

[18] - N=number of subjects evaluable for the outcome measure.

End point values	Figitumumab 20 mg/kg RP2D ESFT	Figitumumab 20 mg/kg RP2D Every 3 Weeks		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9[19]	34[20]		
Units: Hours				
arithmetic mean (standard deviation)	3.441 (± 7.718)	9.394 (± 28.527)		

Notes:

[19] - N=number of subjects evaluable for the outcome measure.

[20] - N=number of subjects evaluable for the outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Observed Plasma Concentration (Tmax) in Cycle 4

End point title	Time to Reach Maximum Observed Plasma Concentration (Tmax) in Cycle 4[21]

End point description:

All subjects treated who had at least 1 of the PK parameters of primary interest in extension cohorts. Summaries for figitumumab 20 mg/kg RP2D, and figitumumab 20 mg/kg RP2D ACC and sarcoma extension cohorts were combined into 1 reporting group: figitumumab 20 mg/kg RP2D every 3 weeks.

End point type	Secondary

End point timeframe:

Cycle 4: 0 (predose), 1, 24 and 72 hours, 7 and 14 days postdose

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Tmax in Cycle 4 was analyzed in subjects of Figitumumab 3 mg/kg , 6 mg/kg , 10 mg/kg , 20 mg/kg , 20 mg/kg (RP2D ESFT), 20 mg/kg (RP2D Every 3 Weeks) reporting arms only.

End point values	Figitumumab 20 mg/kg RP2D ESFT	Figitumumab 20 mg/kg RP2D Every 3 Weeks		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	6[22]	16[23]		
Units: Hours				
arithmetic mean (standard deviation)	4.84 (± 9.436)	7.541 (± 16.343)		

Notes:

[22] - N=number of subjects evaluable for the outcome measure.

[23] - N=number of subjects evaluable for the outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Decay Half-Life (t1/2) in Cycle 1

End point title	Plasma Decay Half-Life (t1/2) in Cycle 1[24]

End point description:

Plasma decay half-life is the time measured for the plasma concentration to decrease by one half. All subjects treated who had at least 1 of the PK parameters of primary interest. Summaries for figitumumab 20 mg/kg RP2D, and figitumumab 20 mg/kg RP2D ACC and sarcoma extension cohorts were combined into 1 reporting group: figitumumab 20 mg/kg RP2D every 3 weeks. Here "99999" in the standard deviation signifies not available (NA). Standard deviation was not calculated as only 1 subject was evaluated.

End point type	Secondary

End point timeframe:

Cycle 1: 0 (predose), 1, 24 and 72 hours, 7 and 14 days postdose

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: t1/2 in Cycle 1 was analyzed in subjects of Figitumumab 3 mg/kg , 6 mg/kg , 10 mg/kg , 20 mg/kg , 20 mg/kg (RP2D ESFT), 20 mg/kg (RP2D Every 3 Weeks) reporting arms only.

End point values	Figitumumab 3 mg/kg	Figitumumab 6 mg/kg	Figitumumab 10 mg/kg	Figitumumab 20 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2[25]	1[26]	3[27]	1[28]
Units: Hours				
arithmetic mean (standard deviation)	203 (± 7.071)	226 (± 99999)	252.3 (± 56.713)	227 (± 99999)

Notes:

[25] - N=number of subjects evaluable for the outcome measure.

[26] - N=number of subjects evaluable for the outcome measure.

[27] - N=number of subjects evaluable for the outcome measure.

[28] - N=number of subjects evaluable for the outcome measure.

End point values	Figitumumab 20 mg/kg RP2D	Figitumumab 20 mg/kg RP2D ESFT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8[29]	2[30]		
Units: Hours				
arithmetic mean (standard deviation)	259.6 (± 80.5)	319 (± 8.485)		

Notes:

[29] - N=number of subjects evaluable for the outcome measure.

[30] - N=number of subjects evaluable for the outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Decay Half-Life (t1/2) in Cycle 4

End point title	Plasma Decay Half-Life (t1/2) in Cycle 4[31]

End point description:

Plasma decay half-life is the time measured for the plasma concentration to decrease by one half. All subjects treated who had at least 1 of the PK parameters of primary interest in extension cohorts. Summaries for figitumumab 20 mg/kg RP2D, and figitumumab 20 mg/kg RP2D ACC and sarcoma extension cohorts were combined into 1 reporting group: figitumumab 20 mg/kg RP2D every 3 weeks.

End point type	Secondary

End point timeframe:

Cycle 4: 0 (predose), 1, 24 and 72 hours, 7 and 14 days postdose

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: t1/2 in Cycle 4 was analyzed in subjects of Figitumumab 3 mg/kg , 6 mg/kg , 10 mg/kg , 20 mg/kg , 20 mg/kg (RP2D ESFT), 20 mg/kg (RP2D Every 3 Weeks) reporting arms only.

End point values	Figitumumab 20 mg/kg RP2D ESFT	Figitumumab 20 mg/kg RP2D Every 3 Weeks		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	3[32]	5[33]		
Units: Hours				
arithmetic mean (standard deviation)	479.7 (± 163.59)	386 (± 172.16)		

Notes:

[32] - N=number of subjects evaluable for the outcome measure.

[33] - N=number of subjects evaluable for the outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Last Quantifiable Concentration (Tlast) in Cycle 1

End point title	Time to Reach Last Quantifiable Concentration (Tlast) in Cycle 1[34]

End point description:

All subjects treated who had at least 1 of the PK parameters of primary interest. Summaries for figitumumab 20 mg/kg RP2D, and figitumumab 20 mg/kg RP2D ACC and sarcoma extension cohorts were combined into 1 reporting group: figitumumab 20 mg/kg RP2D every 3 weeks.

End point type	Secondary

End point timeframe:

Cycle 1: 0 (predose), 1, 24 and 72 hours, 7 and 14 days postdose

Notes:

[34] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: T last in Cycle 1 was analyzed in subjects of Figitumumab 3 mg/kg , 6 mg/kg , 10 mg/kg , 20 mg/kg , 20 mg/kg (RP2D ESFT), 20 mg/kg (RP2D Every 3 Weeks) reporting arms only.

End point values	Figitumumab 3 mg/kg	Figitumumab 6 mg/kg	Figitumumab 10 mg/kg	Figitumumab 20 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[35]	3[36]	3[37]	3[38]
Units: Hours				
arithmetic mean (standard deviation)	501 (± 4.583)	443 (± 96.995)	523.7 (± 41.041)	498.3 (± 1.155)

Notes:

[35] - N=number of subjects evaluable for the outcome measure.

[36] - N=number of subjects evaluable for the outcome measure.

[37] - N=number of subjects evaluable for the outcome measure.

[38] - N=number of subjects evaluable for the outcome measure.

End point values	Figitumumab 20 mg/kg RP2D ESFT	Figitumumab 20 mg/kg RP2D Every 3 Weeks		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9[39]	34[40]		
Units: Hours				
arithmetic mean (standard deviation)	666.7 (± 3.082)	509.5 (± 100.13)		

Notes:

[39] - N=number of subjects evaluable for the outcome measure.

[40] - N=number of subjects evaluable for the outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Last Quantifiable Concentration (Tlast) in Cycle 4

End point title	Time to Reach Last Quantifiable Concentration (Tlast) in Cycle 4[41]

End point description:

All subjects treated who had at least 1 of the PK parameters of primary interest in extension cohorts. Summaries for figitumumab 20 mg/kg RP2D, and figitumumab 20 mg/kg RP2D ACC and sarcoma extension cohorts were combined into 1 reporting group: figitumumab 20 mg/kg RP2D every 3 weeks.

End point type	Secondary

End point timeframe:

Cycle 4: 0 (predose), 1, 24 and 72 hours, 7 and 14 days postdose

Notes:

[41] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: T last in cycle was analyzed in subjects of Figitumumab 3 mg/kg, 6 mg/kg , 10 mg/kg , 20 mg/kg , 20 mg/kg (RP2D ESFT), 20 mg/kg (RP2D Every 3 Weeks) reporting arms only.

End point values	Figitumumab 20 mg/kg RP2D ESFT	Figitumumab 20 mg/kg RP2D Every 3 Weeks		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	6[42]	16[43]		
Units: Hours				
arithmetic mean (standard deviation)	743.7 (± 100.81)	418.7 (± 227.37)		

Notes:

[42] - N=number of subjects evaluable for the outcome measure.

[43] - N=number of subjects evaluable for the outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Systemic Clearance (CL) in Cycle 1

End point title	Systemic Clearance (CL) in Cycle 1[44]

End point description:

CL is a quantitative measure of the rate at which a drug substance is removed from the body. All subjects treated who had at least 1 of the PK parameters of primary interest. Summaries for figitumumab 20 mg/kg RP2D, and figitumumab 20 mg/kg RP2D ACC and sarcoma extension cohorts were combined into 1 reporting group: figitumumab 20 mg/kg RP2D every 3 weeks. Here "99999" in the standard deviation signifies not available (NA). Standard deviation was not calculated as only 1 subject was evaluated.

End point type	Secondary

End point timeframe:

Cycle 1: 0 (predose), 1, 24 and 72 hours, 7 and 14 days postdose

Notes:

[44] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification:

Systemic CL in Cycle 1 was analyzed in subjects of Figitumumab 3 mg/kg , 6 mg/kg , 10 mg/kg , 20 mg /kg , 20 mg/kg (RP2D ESFT), 20 mg/kg (RP2D Every 3 Weeks) reporting arms only.

End point values	Figitumumab 3 mg/kg	Figitumumab 6 mg/kg	Figitumumab 10 mg/kg	Figitumumab 20 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2[45]	1[46]	3[47]	1[48]
Units: milliliter/day/kilogram (mL/day/kg)				
arithmetic mean (standard deviation)	6.435 (± 2.199)	3.6 (± 99999)	4.807 (± 2.059)	4.99 (± 99999)

Notes:

[45] - N=number of subjects evaluable for the outcome measure.

[46] - N=number of subjects evaluable for the outcome measure.

[47] - N=number of subjects evaluable for the outcome measure.

[48] - N=number of subjects evaluable for the outcome measure.

End point values	Figitumumab 20 mg/kg RP2D ESFT	Figitumumab 20 mg/kg RP2D Every 3 Weeks		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	2[49]	7[50]		
Units: milliliter/day/kilogram (mL/day/kg)				
arithmetic mean (standard deviation)	3.155 (± 0.559)	3.846 (± 1.101)		

Notes:

[49] - N=number of subjects evaluable for the outcome measure.

[50] - N=number of subjects evaluable for the outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Systemic Clearance (CL) in Cycle 4

End point title	Systemic Clearance (CL) in Cycle 4[51]

End point description:

CL is a quantitative measure of the rate at which a drug substance is removed from the body. All subjects treated who had at least 1 of the PK parameters of primary interest in extension cohorts. Summaries for figitumumab 20 mg/kg RP2D, and figitumumab 20 mg/kg RP2D ACC and sarcoma extension cohorts were combined into 1 reporting group: figitumumab 20 mg/kg RP2D every 3 weeks.

End point type	Secondary

End point timeframe:

Cycle 4: 0 (predose), 1, 24 and 72 hours, 7 and 14 days postdose

Notes:

[51] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: CL in cycle 4 was analyzed in subjects of Figitumumab 3 mg/kg , 6 mg/kg , 10 mg/kg , 20 mg/kg , 20 mg/kg (RP2D ESFT), 20 mg/kg (RP2D Every 3 Weeks) reporting arms only.

End point values	Figitumumab 20 mg/kg RP2D ESFT	Figitumumab 20 mg/kg RP2D Every 3 Weeks		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	6[52]	6[53]		
Units: mL/day/kg				
arithmetic mean (standard deviation)	2.612 (± 1.112)	2.576 (± 0.484)		

Notes:

[52] - N=number of subjects evaluable for the outcome measure.

[53] - N=number of subjects evaluable for the outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration at End of Infusion (Cendinf) in Cycle 1

End point title	Concentration at End of Infusion (Cendinf) in Cycle 1[54]

End point description:

All subjects treated who had at least 1 of the PK parameters of primary interest. Summaries for figitumumab 20 mg/kg RP2D, and figitumumab 20 mg/kg RP2D ACC and sarcoma extension cohorts were combined into 1 reporting group: figitumumab 20 mg/kg RP2D every 3 weeks.

End point type	Secondary

End point timeframe:

Cycle 1: 0 (predose), 1, 24 and 72 hours, 7 and 14 days postdose

Notes:

[54] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cendinf in cycle 1 was analyzed in subjects of Figitumumab 3 mg/kg , 6 mg/kg , 10 mg/kg , 20 mg/kg , 20 mg/kg (RP2D ESFT), 20 mg/kg (RP2D Every 3 Weeks) reporting arms only.

End point values	Figitumumab 3 mg/kg	Figitumumab 6 mg/kg	Figitumumab 10 mg/kg	Figitumumab 20 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[55]	3[56]	3[57]	3[58]
Units: mg/L				
arithmetic mean (standard deviation)	57.5 (± 3.081)	134.7 (± 31.754)	211 (± 59.808)	463 (± 97.964)

Notes:

[55] - N=number of subjects evaluable for the outcome measure.

[56] - N=number of subjects evaluable for the outcome measure.

[57] - N=number of subjects evaluable for the outcome measure.

[58] - N=number of subjects evaluable for the outcome measure.

End point values	Figitumumab 20 mg/kg RP2D ESFT	Figitumumab 20 mg/kg RP2D Every 3 Weeks		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9[59]	33[60]		
Units: mg/L				
arithmetic mean (standard deviation)	386.3 (± 96.496)	434.3 (± 94.278)		

Notes:

[59] - N=number of subjects evaluable for the outcome measure.

[60] - N=number of subjects evaluable for the outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration at End of Infusion (Cendinf) in Cycle 4

End point title	Concentration at End of Infusion (Cendinf) in Cycle 4[61]

End point description:

All subjects treated who had at least 1 of the PK parameters of primary interest in extension cohorts. Summaries for figitumumab 20 mg/kg RP2D, and figitumumab 20 mg/kg RP2D ACC and sarcoma extension cohorts were combined into 1 reporting group: figitumumab 20 mg/kg RP2D every 3 weeks.

End point type	Secondary

End point timeframe:

Cycle 4: 0 (predose), 1, 24 and 72 hours, 7 and 14 days postdose

Notes:

[61] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cendinf in cycle 4 was analyzed in subjects of Figitumumab 3 mg/kg , 6 mg/kg , 10 mg/kg , 20 mg/kg , 20 mg/kg (RP2D ESFT), 20 mg/kg (RP2D Every 3 Weeks) reporting arms only.

End point values	Figitumumab 20 mg/kg RP2D ESFT	Figitumumab 20 mg/kg RP2D Every 3 Weeks		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	6[62]	16[63]		
Units: mg/L				
arithmetic mean (standard deviation)	650.3 (± 170.8)	685 (± 167.15)		

Notes:

[62] - N=number of subjects evaluable for the outcome measure.

[63] - N=number of subjects evaluable for the outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of Distribution (Vz) in Cycle 1

End point title	Volume of Distribution (Vz) in Cycle 1[64]

End point description:

Vz is defined as the theoretical volume in which the total amount of drug would need to be uniformly distributed to produce the desired blood concentration of a drug. All subjects treated who had at least 1 of the PK parameters of primary interest. Summaries for figitumumab 20 mg/kg RP2D, and figitumumab 20 mg/kg RP2D ACC and sarcoma extension cohorts were combined into 1 reporting group: figitumumab 20 mg/kg RP2D every 3 weeks.Here "99999" in the standard deviation signifies not available (NA). Standard deviation was not calculated as only 1 subject was evaluated.

End point type	Secondary

End point timeframe:

Cycle 1: 0 (predose), 1, 24 and 72 hours, 7 and 14 days postdose

Notes:

[64] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification:
Vz in cycle 1 was analyzed in subjects of Figitumumab 3 mg/kg , 6 mg/kg , 10 mg/kg , 20 mg/kg , 20 m g/kg (RP2D ESFT), 20 mg/kg (RP2D Every
3 Weeks), 20 mg/kg (RP2D ACC+Sarcoma) reporting arms only.

End point values	Figitumumab 3 mg/kg	Figitumumab 6 mg/kg	Figitumumab 10 mg/kg	Figitumumab 20 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2[65]	1[66]	3[67]	1[68]
Units: milliliter/kilogram (mL/kg)				
arithmetic mean (standard deviation)	78 (± 24.183)	49 (± 99999)	70.47 (± 25.733)	68.1 (± 99999)

Notes:

[65] - N=number of subjects evaluable for the outcome measure.

[66] - N=number of subjects evaluable for the outcome measure.

[67] - N=number of subjects evaluable for the outcome measure.

[68] - N=number of subjects evaluable for the outcome measure.

End point values	Figitumumab 20 mg/kg RP2D ESFT	Figitumumab 20 mg/kg RP2D Every 3 Weeks		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	2[69]	7[70]		
Units: milliliter/kilogram (mL/kg)				

arithmetic mean (standard deviation)	60.35 (± 9.122)	59.34 (± 14.36)		

Notes:

[69] - N=number of subjects evaluable for the outcome measure.

[70] - N=number of subjects evaluable for the outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of Distribution (Vz) in Cycle 4

End point title	Volume of Distribution (Vz) in Cycle 4[71]

End point description:

Vz is defined as the theoretical volume in which the total amount of drug would need to be uniformly distributed to produce the desired blood concentration of a drug. All subjects treated who had at least 1 of the PK parameters of primary interest in extension cohorts. Summaries for figitumumab 20 mg/kg RP2D, and figitumumab 20 mg/kg RP2D ACC and sarcoma extension cohorts were combined into 1 reporting group: figitumumab 20 mg/kg RP2D every 3 weeks.

End point type	Secondary

End point timeframe:

Cycle 4: 0 (predose), 1, 24 and 72 hours, 7 and 14 days postdose

Notes:

[71] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification:

Vz in cycle 1 was analyzed in subjects of Figitumumab 3 mg/kg , 6 mg/kg , 10 mg/kg , 20 mg/kg , 20 m g/kg (RP2D ESFT), 20 mg/kg (RP2D Every
3 Weeks), 20 mg/kg (RP2D ACC+Sarcoma) reporting arms only.

End point values	Figitumumab 20 mg/kg RP2D ESFT	Figitumumab 20 mg/kg RP2D Every 3 Weeks		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	3[72]	5[73]		
Units: mL/kg				
arithmetic mean (standard deviation)	89.17 (± 47.461)	61.98 (± 20.741)		

Notes:

[72] - N=number of subjects evaluable for the outcome measure.

[73] - N=number of subjects evaluable for the outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of Distribution at Steady State (Vss) in Cycle 1

End point title	Volume of Distribution at Steady State (Vss) in Cycle 1[74]

End point description:

Vz is defined as the theoretical volume in which the total amount of drug would need to be uniformly distributed to produce the desired blood concentration of a drug. Vss is the Vz at steady-state. All subjects treated who had at least 1 of the PK parameters of primary interest. Summaries for figitumumab 20 mg/kg RP2D, and figitumumab 20 mg/kg RP2D ACC and sarcoma extension cohorts were combined into 1 reporting group: figitumumab 20 mg/kg RP2D every 3 weeks. Here "99999" in the standard deviation signifies not available (NA). Standard deviation was not calculated as only 1 subject

was evaluated.

End point type	Secondary

End point timeframe:

Cycle 1: 0 (predose), 1, 24 and 72 hours, 7 and 14 days postdose

Notes:

[74] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification:
Vss in Cycle 1 was analyzed in subjects of Figitumumab 3 mg/kg , 6 mg/kg , 10 mg/kg , 20 mg/kg , 20 mg/kg (RP2D ESFT), 20 mg/kg (RP2D Every 3 Weeks) reporting arms only.

End point values	Figitumumab 3 mg/kg	Figitumumab 6 mg/kg	Figitumumab 10 mg/kg	Figitumumab 20 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2[75]	1[76]	3[77]	1[78]
Units: mL/kg				
arithmetic mean (standard deviation)	75.05 (± 20.011)	47.9 (± 99999)	68.8 (± 23.477)	66.9 (± 99999)

Notes:

[75] - N=number of subjects evaluable for the outcome measure.

[76] - N=number of subjects evaluable for the outcome measure.

[77] - N=number of subjects evaluable for the outcome measure.

[78] - N=number of subjects evaluable for the outcome measure.

End point values	Figitumumab 20 mg/kg RP2D ESFT	Figitumumab 20 mg/kg RP2D Every 3 Weeks		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	2[79]	7[80]		
Units: mL/kg				
arithmetic mean (standard deviation)	61.65 (± 6.435)	59.27 (± 14.765)		

Notes:

[79] - N=number of subjects evaluable for the outcome measure.

[80] - N=number of subjects evaluable for the outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of Distribution at Steady State (Vss) in Cycle 4

End point title	Volume of Distribution at Steady State (Vss) in Cycle 4[81]

End point description:

Vz is defined as the theoretical volume in which the total amount of drug would need to be uniformly distributed to produce the desired blood concentration of a drug. Vss is the Vz at steady-state. All subjects treated who had at least 1 of the PK parameters of primary interest in extension cohorts. Summaries for figitumumab 20 mg/kg RP2D, and figitumumab 20 mg/kg RP2D ACC and sarcoma extension cohorts were combined into 1 reporting group: figitumumab 20 mg/kg RP2D every 3 weeks.

End point type	Secondary

End point timeframe:

Cycle 4: 0 (predose), 1, 24 and 72 hours, 7 and 14 days postdose

Notes:

[81] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification:
Vss in Cycle 4 was analyzed in subjects of Figitumumab 3 mg/kg , 6 mg/kg , 10 mg/kg , 20 mg/kg , 20 mg/kg (RP2D ESFT), 20 mg/kg (RP2D Every 3 Weeks) reporting arms only.

End point values	Figitumumab 20 mg/kg RP2D ESFT	Figitumumab 20 mg/kg RP2D Every 3 Weeks		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	3[82]	5[83]		
Units: mL/kg				
arithmetic mean (standard deviation)	86.07 (± 42.133)	60.84 (± 19.694)		

Notes:

[82] - N=number of subjects evaluable for the outcome measure.

[83] - N=number of subjects evaluable for the outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Curve From Time Zero to Last Quantifiable Concentration (AUClast) in Cycle 1

End point title	Area Under the Curve From Time Zero to Last Quantifiable Concentration (AUClast) in Cycle 1[84]

End point description:

Area under the plasma concentration time-curve from zero to the last measured concentration. All subjects treated who had at least 1 of the PK parameters of primary interest. Summaries for figitumumab 20 mg/kg RP2D, and figitumumab 20 mg/kg RP2D ACC and sarcoma extension cohorts were combined into 1 reporting group: figitumumab 20 mg/kg RP2D every 3 weeks.

End point type	Secondary

End point timeframe:

Cycle 1: 0 (predose), 1, 24 and 72 hours, 7 and 14 days postdose

Notes:

[84] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification:
Data for AUClast in cycle 1 was analyzed in subjects in Figitumumab 3 mg/kg , 6 mg/kg , 10 mg/kg , 20 mg/kg , 20 mg/kg (RP2D ESFT), 20 mg/kg (RP2D Every 3 Weeks) reporting groups only.

End point values	Figitumumab 3 mg/kg	Figitumumab 6 mg/kg	Figitumumab 10 mg/kg	Figitumumab 20 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[85]	2[86]	3[87]	3[88]
Units: milligram*hour/liter (mg*hr/L)				
arithmetic mean (standard deviation)	10900 (± 3005)	27500 (± 5656.9)	43900 (± 19630)	89430 (± 11904)

Notes:

[85] - N=number of subjects evaluable for the outcome measure.

[86] - N=number of subjects evaluable for the outcome measure.

[87] - N=number of subjects evaluable for the outcome measure.

[88] - N=number of subjects evaluable for the outcome measure.

End point values	Figitumumab 20 mg/kg RP2D ESFT	Figitumumab 20 mg/kg RP2D Every 3 Weeks		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9[89]	31[90]		
Units: milligram*hour/liter (mg*hr/L)				
arithmetic mean (standard deviation)	102700 (± 25300)	107900 (± 36398)		

Notes:

[89] - N=number of subjects evaluable for the outcome measure.

[90] - N=number of subjects evaluable for the outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Curve From Time Zero to Last Quantifiable Concentration (AUClast) in Cycle 4

End point title	Area Under the Curve From Time Zero to Last Quantifiable Concentration (AUClast) in Cycle 4[91]

End point description:

Area under the plasma concentration time-curve from zero to the last measured concentration. All subjects treated who had at least 1 of the PK parameters of primary interest in extension cohorts. Summaries for figitumumab 20 mg/kg RP2D, and figitumumab 20 mg/kg RP2D ACC and sarcoma extension cohorts were combined into 1 reporting group: figitumumab 20 mg/kg RP2D every 3 weeks.

End point type	Secondary

End point timeframe:

Cycle 4: 0 (predose), 1, 24 and 72 hours, 7 and 14 days postdose

Notes:

[91] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: AUClast in Cycle 4 was analyzed in subjects of Figitumumab 3 mg/kg , 6 mg/kg , 10 mg/kg , 20 mg/kg , 20 mg/kg (RP2D ESFT), 20 mg/kg (RP2D Every 3 Weeks) reporting arms only.

End point values	Figitumumab 20 mg/kg RP2D ESFT	Figitumumab 20 mg/kg RP2D Every 3 Weeks		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	6[92]	16[93]		
Units: mg*hr/L				
arithmetic mean (standard deviation)	214500 (± 67592)	166500 (± 77400)		

Notes:

[92] - N=number of subjects evaluable for the outcome measure.

[93] - N=number of subjects evaluable for the outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Curve From Time Zero to Extrapolated Infinite Time [AUC (0 - ∞)] in Cycle 1

End point title	Area Under the Curve From Time Zero to Extrapolated Infinite Time [AUC (0 - ∞)] in Cycle 1[94]

End point description:

Area under the plasma concentration versus time curve from time zero (pre-dose) to extrapolated infinite time (0 - ∞). All subjects treated who had at least 1 of the PK parameters of primary interest. Summaries for figitumumab 20 mg/kg RP2D, and figitumumab 20 mg/kg RP2D ACC and sarcoma extension cohorts were combined into 1 reporting group: figitumumab 20 mg/kg RP2D every 3 weeks. Here "99999" in the standard deviation signifies not available (NA). Standard deviation was not calculated as only 1 subject was evaluated.

End point type	Secondary

End point timeframe:

Cycle 1: 0 (predose), 1, 24 and 72 hours, 7 and 14 days postdose

Notes:

[94] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification:
AUC (0 ∞) in Cycle 1 was analyzed in subjects of Figitumumab 3 mg/kg , 6 mg/kg , 10 mg/kg , 20 mg/kg , 20 mg/kg (RP2D ESFT), 20 mg/kg (RP2D Every 3 Weeks) reporting arms only.

End point values	Figitumumab 3 mg/kg	Figitumumab 6 mg/kg	Figitumumab 10 mg/kg	Figitumumab 20 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2[95]	1[96]	3[97]	1[98]
Units: mg*hr/L				
arithmetic mean (standard deviation)	11910 (± 4094.1)	40000 (± 99999)	57770 (± 28167)	96300 (± 99999)

Notes:

[95] - N=number of subjects evaluable for the outcome measure.

[96] - N=number of subjects evaluable for the outcome measure.

[97] - N=number of subjects evaluable for the outcome measure.

[98] - N=number of subjects evaluable for the outcome measure.

End point values	Figitumumab 20 mg/kg RP2D ESFT	Figitumumab 20 mg/kg RP2D Every 3 Weeks		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	2[99]	7[100]		
Units: mg*hr/L				
arithmetic mean (standard deviation)	154500 (± 27577)	136000 (± 47622)		

Notes:

[99] - N=number of subjects evaluable for the outcome measure.

[100] - N=number of subjects evaluable for the outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-time Profile From Time 0 to 504 Hours (21 Days) (AUC504) in Cycle 1

End point title	Area Under the Plasma Concentration-time Profile From Time 0 to 504 Hours (21 Days) (AUC504) in Cycle 1[101]

End point description:

All subjects treated who had at least 1 of the PK parameters of primary interest in all cohorts except ESFT extension cohort. Summaries for figitumumab 20 mg/kg RP2D, and RP2D ACC and sarcoma extension cohorts were combined into 1 reporting group: 20 mg/kg RP2D every 3 weeks.

End point type	Secondary

End point timeframe:

Cycle 1: 0 (predose), 1, 24 and 72 hours, 7 and 14 days postdose

Notes:

[101] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification:
AUC 504 in Cycle 1 was analyzed in subjects of Figitumumab 3, 6, 10, 20 mg/kg reporting arms only.

End point values	Figitumumab 3 mg/kg	Figitumumab 6 mg/kg	Figitumumab 10 mg/kg	Figitumumab 20 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[102]	2[103]	3[104]	3[105]
Units: mg*hr/L				
arithmetic mean (standard deviation)	10900 (± 3005)	27500 (± 5656.9)	43170 (± 20124)	89430 (± 11904)

Notes:

[102] - N=number of subjects evaluable for the outcome measure.

[103] - N=number of subjects evaluable for the outcome measure.

[104] - N=number of subjects evaluable for the outcome measure.

[105] - N=number of subjects evaluable for the outcome measure.

End point values	Figitumumab 20 mg/kg RP2D Every 3 Weeks			
Subject group type	Subject analysis set			
Number of subjects analysed	31[106]			
Units: mg*hr/L				
arithmetic mean (standard deviation)	104000 (± 32547)			

Notes:

[106] - N=number of subjects evaluable for the outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-time Profile From Time 0 to 504 Hours (21 Days) (AUC504) in Cycle 4

End point title	Area Under the Plasma Concentration-time Profile From Time 0 to 504 Hours (21 Days) (AUC504) in Cycle 4

End point description:

All subjects treated who had at least 1 of the PK parameters of primary interest in all cohorts except ESFT extension cohort. Summaries for figitumumab 20 mg/kg RP2D, and RP2D ACC and sarcoma extension cohorts were combined into 1 reporting group: 20 mg/kg RP2D every 3 weeks.

End point type	Secondary

End point timeframe:

Cycle 4: 0 (predose), 1, 24 and 72 hours, 7 and 14 days postdose

End point values	Figitumumab 20 mg/kg RP2D Every 3 Weeks			
Subject group type	Subject analysis set			
Number of subjects analysed	9[107]			
Units: mg*hr/L				
arithmetic mean (standard deviation)	193100 (± 40001)			

Notes:

[107] - N=number of subjects evaluable for the outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-time Profile From Time 0 to 672 Hours (28 Days) (AUC672) in Cycle 1

End point title	Area Under the Plasma Concentration-time Profile From Time 0 to 672 Hours (28 Days) (AUC672) in Cycle 1[108]

End point description:

All subjects treated who had at least 1 of the PK parameters of primary interest in RP2D ESFT extension cohort.

End point type	Secondary

End point timeframe:

Cycle 1: 0 (predose), 1, 24 and 72 hours, 7 and 14 days postdose

Notes:

[108] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Tmax in Cycle 4 was analyzed in subjects of Figitumumab 20 mg/kg RP2D ESFT reporting arm only.

End point values	Figitumumab 20 mg/kg RP2D ESFT			
Subject group type	Reporting group			
Number of subjects analysed	9[109]			
Units: mg*hr/L				
arithmetic mean (standard deviation)	102400 (± 25227)			

Notes:

[109] - N=number of subjects evaluable for the outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-time Profile From Time 0 to 672 Hours (28 Days) (AUC672) in Cycle 4

End point title	Area Under the Plasma Concentration-time Profile From Time 0 to 672 Hours (28 Days) (AUC672) in Cycle 4[110]

End point description:

All subjects treated who had at least 1 of the PK parameters of primary interest in RP2D ESFT extension cohort.

End point type	Secondary

End point timeframe:

Cycle 4: 0 (predose), 1, 24 and 72 hours, 7 and 14 days postdose

Notes:

[110] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification:
Tmax in Cycle 4 was analyzed in subjects of Figitumumab 20 mg/kg RP2D ESFT reporting arm only.

End point values	Figitumumab 20 mg/kg RP2D ESFT			
Subject group type	Reporting group			
Number of subjects analysed	6[111]			
Units: mg*hr/L				
arithmetic mean (standard deviation)	207200 (± 72334)			

Notes:

[111] - N=number of subjects evaluable for the outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Human Anti-human Antibodies (HAHA) Levels

End point title	Human Anti-human Antibodies (HAHA) Levels[112]

End point description:

HAHA were indicators of immunogenicity to figitumumab. Per protocol, the presence of HAHA would only be evaluated for those samples with plasma figitumumab concentrations below the limit of quantification (BLQ). Since none of the postdose samples in the study had figitumumab concentrations BLQ, therefore no sample was analyzed for HAHA.

End point type	Secondary

End point timeframe:

30 minutes predose in Cycles 1 up to 61, and last scheduled follow-up visit (up to 150 days from the last dose of study drug)

Notes:

[112] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: HAHA levels were analyzed in subjects of Figitumumab 3, 6, 10, 20 mg/kg reporting arms only.

End point values	Figitumumab 3 mg/kg	Figitumumab 6 mg/kg	Figitumumab 10 mg/kg	Figitumumab 20 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[113]	0[114]	0[115]	0[116]
Units: subjects				
number (not applicable)				

Notes:

[113] - No sample in the study had figitumumab concentrations BLQ therefore no sample was analyzed for HAHA.
[114] - No sample in the study had figitumumab concentrations BLQ therefore no sample was analyzed for HAHA.
[115] - No sample in the study had figitumumab concentrations BLQ therefore no sample was analyzed for HAHA.

[116] - No sample in the study had figitumumab concentrations BLQ therefore no sample was analyzed for HAHA.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Circulating Tumor Cells (CTCs)

End point title	Number of Circulating Tumor Cells (CTCs)[117]

End point description:

Quantification of CTCs using an automated microscope system. Pretreatment CTCs were detected in an insufficient number of subjects to analyze for any treatment effect on this pharmacodynamic biomarker.

End point type	Secondary

End point timeframe:

30 minutes predose in all cycles (up to 17); 1, 3, 7, and 14 days postdose in Cycle 1 for dose escalation and RP2D extension cohorts; and also 1 day postdose in Cycle 4 for RP2D extension cohort

Notes:

[117] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification:
Number of CTCs was analyzed in subjects of Figitumumab 3, 6, 10, 20 mg/kg, 20 mg/kg (RP2D Every 3 Weeks) reporting arms only.

End point values	Figitumumab 3 mg/kg	Figitumumab 6 mg/kg	Figitumumab 10 mg/kg	Figitumumab 20 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[118]	0[119]	0[120]	0[121]
Units: subjects				
number (not applicable)				

Notes:

[118] - Insufficient number of subjects to analyze for treatment effect on this pharmacodynamic biomarker.
[119] - Insufficient number of subjects to analyze for treatment effect on this pharmacodynamic biomarker.
[120] - Insufficient number of subjects to analyze for treatment effect on this pharmacodynamic biomarker.
[121] - Insufficient number of subjects to analyze for treatment effect on this pharmacodynamic biomarker.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Insulin-like Growth Factor 1 Receptor (IGF-1R) Positive CTCs

End point title	Number of Insulin-like Growth Factor 1 Receptor (IGF-1R) Positive CTCs[122]

End point description:

Quantification of IGF-IR positive CTCs using an automated microscope system. Pretreatment IGF-1R positive CTCs were detected in an insufficient number of subjects to analyze for any treatment effect on this pharmacodynamic biomarker.

End point type	Secondary

End point timeframe:

30 minutes predose in all cycles (up to 17); 1, 3, 7, and 14 days postdose in Cycle 1 for dose escalation and RP2D extension cohorts; and also 1 day postdose in Cycle 4 for RP2D extension cohort

Notes:

[122] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: IGF-
1R Positive CTCs was analyzed in subjects of Figitumumab 3, 6, 10, 20 mg/kg reporting arms only.

End point values	Figitumumab 3 mg/kg	Figitumumab 6 mg/kg	Figitumumab 10 mg/kg	Figitumumab 20 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[123]	0[124]	0[125]	0[126]
Units: subjects				
number (not applicable)				

Notes:

[123] - Insufficient number of subjects to analyze for treatment effect on this pharmacodynamic biomarker.
[124] - Insufficient number of subjects to analyze for treatment effect on this pharmacodynamic biomarker.
[125] - Insufficient number of subjects to analyze for treatment effect on this pharmacodynamic biomarker.
[126] - Insufficient number of subjects to analyze for treatment effect on this pharmacodynamic biomarker.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment emergent adverse events are reported from time of first dose of study treatment up to 150 days after last dose of study treatment .

Adverse event reporting additional description:

The same event may appear as both an adverse event (AE) and a serious AE (SAE). However, what is presented are distinct events. An event may be categorized as serious in one subject and as nonserious in another subject, or one subject may have experienced both a serious and nonserious event during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	10MG/KG

Reporting group description:

Figitumumab 3 mg/kg was supplied as a liquid solution administered as an IV infusion over 2.5 hours (plus or minus 15 minutes) on Day 1 of each cycle (3 weeks in duration) for dose escalation cohort.

Reporting group title	20MG/KG

Reporting group description:

Figitumumab 20 mg/kg was supplied as a liquid solution administered as an IV infusion over 2.5 hours (plus or minus 15 minutes) on Day 1 of each cycle (3 weeks in duration) for dose escalation cohort.

Reporting group title	20MG/KG RP2D

Reporting group description:

Figitumumab 20 mg/kg was supplied as a liquid solution administered as an IV infusion over 2.5 hours (plus or minus 15 minutes) on Day 1 of each cycle (3 weeks in duration) for RP2D extension cohort.

Reporting group title	20MG/KG RP2D ACC+SARCOMA

Reporting group description:

Figitumumab 20 mg/kg was supplied as a liquid solution administered as an IV infusion over 2.5 hours (plus or minus 15 minutes) on Day 1 of each cycle (3 weeks in duration) for RP2D ACC and sarcoma extension cohort.

Reporting group title	20MG/KG RP2D ESFT

Reporting group description:

Figitumumab 20 mg/kg was supplied as a liquid solution administered as an IV infusion over 2.5 hours (plus or minus 15 minutes) on Day 1 of each cycle (4 weeks in duration) for RP2D ESFT extension cohort.

Reporting group title	3MG/KG

Reporting group description:

Figitumumab 3 mg/kg was supplied as a liquid solution administered as an IV infusion over 2.5 hours (plus or minus 15 minutes) on Day 1 of each cycle (3 weeks in duration) for dose escalation cohort.

Reporting group title	6MG/KG

Reporting group description:

Figitumumab 6 mg/kg was supplied as a liquid solution administered as an IV infusion over 2.5 hours (plus or minus 15 minutes) on Day 1 of each cycle (3 weeks in duration) for dose escalation cohort.

Serious adverse events	10MG/KG	20MG/KG	20MG/KG RP2D
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	1 / 3 (33.33%)	5 / 13 (38.46%)
number of deaths (all causes)	3	1	3

number of deaths resulting from adverse events	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (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 creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (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 culture positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (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 uric acid increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (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
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (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
Haemoglobin decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (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
Vascular disorders			
Superior vena cava occlusion			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (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
Thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (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			
Headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (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
Intracranial pressure increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (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
Spinal cord compression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (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 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (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
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (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 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disease progression			
subjects affected / exposed	3 / 3 (100.00%)	1 / 3 (33.33%)	2 / 13 (15.38%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 6
deaths causally related to treatment / all	0 / 3	0 / 1	0 / 2
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (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
Ileus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (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
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (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
Intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Reproductive system and breast			

disorders			
Female genital tract fistula			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (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
Pneumomediastinum			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure acute			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (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			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (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 pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (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			
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (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
Lower respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (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
Lower respiratory tract infection viral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (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
Staphylococcal infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	20MG/KG RP2D	20MG/KG RP2D	3MG/KG

	ACC+SARCOMA	ESFT	
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 29 (58.62%)	5 / 11 (45.45%)	2 / 3 (66.67%)
number of deaths (all causes)	8	4	1
number of deaths resulting from adverse events	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (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
Blood creatinine increased			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood culture positive			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (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
Blood uric acid increased			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (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
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (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
Haemoglobin decreased			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (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

Vascular disorders			
Superior vena cava occlusion			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (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
Thrombosis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (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
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	6 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial pressure increased			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (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 disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (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
Oedema peripheral			

subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (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
Pyrexia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disease progression			
subjects affected / exposed	8 / 29 (27.59%)	3 / 11 (27.27%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 13	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 8	0 / 3	0 / 1
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (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
Ileus			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (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
Nausea			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (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
Vomiting			
subjects affected / exposed	1 / 29 (3.45%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			

subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (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
Reproductive system and breast disorders			
Female genital tract fistula			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (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
Pneumomediastinum			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (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			
Proteinuria			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure acute			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (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
Renal pain			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (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
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (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
Bone pain			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (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
Musculoskeletal pain			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (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 in extremity			
subjects affected / exposed	1 / 29 (3.45%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (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
Lower respiratory tract infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (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
Lower respiratory tract infection viral			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (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
Pneumonia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (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
Staphylococcal infection			

subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	6MG/KG		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood culture positive			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood uric acid increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Haemoglobin decreased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Superior vena cava occlusion			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombosis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intracranial pressure increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal cord compression			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oedema peripheral				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Disease progression				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Gastrointestinal disorders				
Ascites				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ileus				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				

subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Female genital tract fistula			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumomediastinum			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal failure acute			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal pain			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection viral			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Staphylococcal infection			
subjects affected / exposed	0 / 3 (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	10MG/KG	20MG/KG	20MG/KG RP2D
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	13 / 13 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Skin papilloma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Hot flush			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	4
Hypotension			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Pallor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Tooth repair			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Catheter site related reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Catheter site pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Crepitations			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Disease progression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	3 / 3 (100.00%)	6 / 13 (46.15%)
occurrences (all)	0	5	8
Feeling abnormal			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	3
Gait disturbance			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Localised oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Mass			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Immune system disorders			
Graft versus host disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Seasonal allergy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0

Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Pelvic pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Scrotal pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	4
Dyspnoea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	3 / 13 (23.08%)
occurrences (all)	1	0	3
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	3
Haemoptysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Nasal discomfort			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Pneumonitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Pneumothorax			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Adjustment disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Anxiety			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Depressed mood			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0

Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	3
Activated partial thromboplastin time abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	5 / 13 (38.46%)
occurrences (all)	0	0	10
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	7 / 13 (53.85%)
occurrences (all)	3	0	8
Bacterial test positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Blood creatinine increased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 13 (7.69%)
occurrences (all)	1	1	1
Blood glucose increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Blood phosphorus decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Blood magnesium increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Blood potassium decreased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Blood sodium decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Blood potassium increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Blood uric acid increased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	3 / 13 (23.08%)
occurrences (all)	1	2	5
Blood urea increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Body temperature			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Fungal test positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	5 / 13 (38.46%)
occurrences (all)	2	0	7
Haemoglobin decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
International normalised ratio increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Neutrophil count increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Platelet count decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Pulse abnormal			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Urine leukocyte esterase positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Infusion related reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Procedural pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Scratch			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Wound dehiscence			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	5
Dizziness postural			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Headache			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 13 (7.69%)
occurrences (all)	0	2	2
Hyporeflexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Paraesthesia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Paralysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Sinus headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Phantom pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	3
Lymphopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Ear and labyrinth disorders			
Ear congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Tinnitus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	2
Eye pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Eye pruritus			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Keratitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Miosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences (all)	1	2	0
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Cheilitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 13 (23.08%)
occurrences (all)	0	0	4
Dental caries			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	2 / 3 (66.67%)	1 / 3 (33.33%)	6 / 13 (46.15%)
occurrences (all)	2	1	7

Dry mouth			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 13 (23.08%)
occurrences (all)	0	0	3
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Dysphagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Mouth haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	8 / 13 (61.54%)
occurrences (all)	2	0	14
Oesophageal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1

Sensitivity of teeth			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Tooth disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Vomiting			
subjects affected / exposed	2 / 3 (66.67%)	1 / 3 (33.33%)	6 / 13 (46.15%)
occurrences (all)	2	1	9
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Alopecia totalis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Blister			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Blood blister			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Dermal cyst			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Eczema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Nail disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Hyperhidrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Onychoclasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Petechiae			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	0 / 13 (0.00%)
occurrences (all)	1	3	0
Skin irritation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Skin discolouration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Skin mass			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Azotaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Microalbuminuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	0 / 13 (0.00%)
occurrences (all)	0	3	0
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Renal impairment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Urinary incontinence			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Delayed puberty			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Goitre			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	3
Groin pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Limb discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 13 (23.08%)
occurrences (all)	0	0	3
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	5
Musculoskeletal stiffness			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Osteonecrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Trismus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Eye infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Nail infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0

Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Staphylococcal infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Subcutaneous abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Tinea pedis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	4
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0

Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 3 (66.67%)	2 / 3 (66.67%)	5 / 13 (38.46%)
occurrences (all)	3	2	9
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	3 / 3 (100.00%)	5 / 13 (38.46%)
occurrences (all)	0	5	15
Hyperlipidaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Hypermagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	2 / 13 (15.38%)
occurrences (all)	0	1	2
Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Hyperuricaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	4
Hypoglycaemia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	20MG/KG RP2D ACC+SARCOMA	20MG/KG RP2D ESFT	3MG/KG
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 29 (96.55%)	11 / 11 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin papilloma			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 29 (3.45%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Haematoma			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypertension			

subjects affected / exposed	4 / 29 (13.79%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	8	1	0
Hypotension			
subjects affected / exposed	1 / 29 (3.45%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Pallor			
subjects affected / exposed	3 / 29 (10.34%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	3	1	0
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Tooth repair			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Catheter site related reaction			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Catheter site pain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Chest pain			
subjects affected / exposed	4 / 29 (13.79%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	6	2	0
Chills			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Crepitations			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Disease progression			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Fatigue			

subjects affected / exposed	12 / 29 (41.38%)	7 / 11 (63.64%)	0 / 3 (0.00%)
occurrences (all)	21	13	0
Feeling abnormal			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Influenza like illness			
subjects affected / exposed	3 / 29 (10.34%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	4	1	0
Gait disturbance			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Localised oedema			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	6	0
Mass			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Mucosal inflammation			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	3 / 29 (10.34%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	5	1	0
Pain			
subjects affected / exposed	0 / 29 (0.00%)	3 / 11 (27.27%)	1 / 3 (33.33%)
occurrences (all)	0	3	2
Pyrexia			
subjects affected / exposed	1 / 29 (3.45%)	4 / 11 (36.36%)	0 / 3 (0.00%)
occurrences (all)	1	4	0
Immune system disorders			
Graft versus host disease			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	3	0

Seasonal allergy			
subjects affected / exposed	0 / 29 (0.00%)	2 / 11 (18.18%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pelvic pain			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Scrotal pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Dysphonia			
subjects affected / exposed	0 / 29 (0.00%)	2 / 11 (18.18%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Cough			
subjects affected / exposed	3 / 29 (10.34%)	5 / 11 (45.45%)	1 / 3 (33.33%)
occurrences (all)	3	13	1
Dyspnoea			
subjects affected / exposed	4 / 29 (13.79%)	5 / 11 (45.45%)	0 / 3 (0.00%)
occurrences (all)	5	8	0
Epistaxis			
subjects affected / exposed	1 / 29 (3.45%)	4 / 11 (36.36%)	1 / 3 (33.33%)
occurrences (all)	1	5	1
Haemoptysis			
subjects affected / exposed	2 / 29 (6.90%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Hypoxia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			

subjects affected / exposed	0 / 29 (0.00%)	2 / 11 (18.18%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Nasal discomfort			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	2 / 29 (6.90%)	3 / 11 (27.27%)	0 / 3 (0.00%)
occurrences (all)	2	14	0
Pneumonitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pneumothorax			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rhinitis allergic			
subjects affected / exposed	0 / 29 (0.00%)	2 / 11 (18.18%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Rhinorrhoea			
subjects affected / exposed	1 / 29 (3.45%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Sinus congestion			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Wheezing			
subjects affected / exposed	0 / 29 (0.00%)	2 / 11 (18.18%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Psychiatric disorders			
Adjustment disorder			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	2 / 29 (6.90%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Depressed mood			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	2	0

Depression			
subjects affected / exposed	2 / 29 (6.90%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	3	2	0
Insomnia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	2 / 29 (6.90%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Activated partial thromboplastin time abnormal			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	6 / 29 (20.69%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	12	2	0
Aspartate aminotransferase increased			
subjects affected / exposed	7 / 29 (24.14%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	10	1	0
Bacterial test positive			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood alkaline phosphatase increased			
subjects affected / exposed	4 / 29 (13.79%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	7	0	0
Blood creatinine increased			
subjects affected / exposed	4 / 29 (13.79%)	1 / 11 (9.09%)	1 / 3 (33.33%)
occurrences (all)	7	3	2
Blood glucose increased			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood magnesium increased			

subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Blood potassium decreased			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Blood sodium decreased			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood potassium increased			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood uric acid increased			
subjects affected / exposed	5 / 29 (17.24%)	1 / 11 (9.09%)	1 / 3 (33.33%)
occurrences (all)	5	1	1
Blood urea increased			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Body temperature			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Fungal test positive			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	7 / 29 (24.14%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	11	1	0
Haemoglobin decreased			
subjects affected / exposed	3 / 29 (10.34%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	3	1	0
International normalised ratio increased			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Neutrophil count decreased			

subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Neutrophil count increased			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Pulse abnormal			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	3 / 29 (10.34%)	2 / 11 (18.18%)	0 / 3 (0.00%)
occurrences (all)	8	3	0
Urine leukocyte esterase positive			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Weight increased			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
White blood cell count decreased			
subjects affected / exposed	2 / 29 (6.90%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	1 / 29 (3.45%)	1 / 11 (9.09%)	1 / 3 (33.33%)
occurrences (all)	3	1	1
Infusion related reaction			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Ligament sprain			

subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Procedural pain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Scratch			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Wound dehiscence			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 29 (3.45%)	2 / 11 (18.18%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 29 (13.79%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	4	1	0
Dizziness postural			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	1 / 29 (3.45%)	2 / 11 (18.18%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Headache			
subjects affected / exposed	6 / 29 (20.69%)	4 / 11 (36.36%)	0 / 3 (0.00%)
occurrences (all)	8	27	0
Hyporeflexia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Lethargy			
subjects affected / exposed	1 / 29 (3.45%)	2 / 11 (18.18%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Neuropathy peripheral			

subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Paralysis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Sinus headache			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Phantom pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 29 (10.34%)	1 / 11 (9.09%)	1 / 3 (33.33%)
occurrences (all)	7	1	2
Lymphopenia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear congestion			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Ear pain			
subjects affected / exposed	0 / 29 (0.00%)	2 / 11 (18.18%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Tinnitus			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Eye pain			

subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Eye pruritus			
subjects affected / exposed	0 / 29 (0.00%)	2 / 11 (18.18%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Keratitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Miosis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 29 (0.00%)	2 / 11 (18.18%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Vision blurred			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	3 / 29 (10.34%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	3	1	0
Abdominal pain			
subjects affected / exposed	1 / 29 (3.45%)	2 / 11 (18.18%)	0 / 3 (0.00%)
occurrences (all)	1	10	0
Abdominal pain upper			
subjects affected / exposed	0 / 29 (0.00%)	2 / 11 (18.18%)	0 / 3 (0.00%)
occurrences (all)	0	6	0
Cheilitis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	9 / 29 (31.03%)	4 / 11 (36.36%)	1 / 3 (33.33%)
occurrences (all)	11	7	2
Dental caries			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Diarrhoea			
subjects affected / exposed	5 / 29 (17.24%)	7 / 11 (63.64%)	0 / 3 (0.00%)
occurrences (all)	5	14	0
Dry mouth			
subjects affected / exposed	4 / 29 (13.79%)	0 / 11 (0.00%)	1 / 3 (33.33%)
occurrences (all)	4	0	1
Dyspepsia			
subjects affected / exposed	0 / 29 (0.00%)	3 / 11 (27.27%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Dysphagia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Flatulence			
subjects affected / exposed	3 / 29 (10.34%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gingival bleeding			
subjects affected / exposed	1 / 29 (3.45%)	2 / 11 (18.18%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Haematochezia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Mouth haemorrhage			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Nausea			
subjects affected / exposed	13 / 29 (44.83%)	4 / 11 (36.36%)	0 / 3 (0.00%)
occurrences (all)	17	16	0
Oesophageal pain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Oral pain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Rectal haemorrhage			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sensitivity of teeth			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	3 / 29 (10.34%)	0 / 11 (0.00%)	1 / 3 (33.33%)
occurrences (all)	4	0	1
Tooth disorder			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	0 / 29 (0.00%)	2 / 11 (18.18%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Vomiting			
subjects affected / exposed	6 / 29 (20.69%)	7 / 11 (63.64%)	1 / 3 (33.33%)
occurrences (all)	6	20	1
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	3 / 29 (10.34%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Alopecia totalis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blister			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood blister			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dermal cyst			

subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dermatitis contact			
subjects affected / exposed	2 / 29 (6.90%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Dry skin			
subjects affected / exposed	1 / 29 (3.45%)	2 / 11 (18.18%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Eczema			
subjects affected / exposed	0 / 29 (0.00%)	2 / 11 (18.18%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Erythema			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nail disorder			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hyperhidrosis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Onychoclasis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Petechiae			
subjects affected / exposed	2 / 29 (6.90%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Pruritus			
subjects affected / exposed	0 / 29 (0.00%)	2 / 11 (18.18%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Rash			
subjects affected / exposed	2 / 29 (6.90%)	2 / 11 (18.18%)	0 / 3 (0.00%)
occurrences (all)	2	3	0
Skin irritation			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin discolouration			

subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin mass			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Urticaria			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Azotaemia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	1 / 29 (3.45%)	1 / 11 (9.09%)	1 / 3 (33.33%)
occurrences (all)	1	6	1
Dysuria			
subjects affected / exposed	1 / 29 (3.45%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Microalbuminuria			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pollakiuria			
subjects affected / exposed	2 / 29 (6.90%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Proteinuria			
subjects affected / exposed	3 / 29 (10.34%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	4	1	0
Renal impairment			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Delayed puberty			

subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Goitre			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypothyroidism			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 29 (3.45%)	5 / 11 (45.45%)	1 / 3 (33.33%)
occurrences (all)	1	18	2
Back pain			
subjects affected / exposed	7 / 29 (24.14%)	4 / 11 (36.36%)	0 / 3 (0.00%)
occurrences (all)	10	20	0
Groin pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Flank pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Limb discomfort			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	5 / 29 (17.24%)	6 / 11 (54.55%)	0 / 3 (0.00%)
occurrences (all)	6	30	0
Muscular weakness			
subjects affected / exposed	4 / 29 (13.79%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	4	1	0
Musculoskeletal chest pain			
subjects affected / exposed	2 / 29 (6.90%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Musculoskeletal pain			

subjects affected / exposed	3 / 29 (10.34%)	3 / 11 (27.27%)	0 / 3 (0.00%)
occurrences (all)	3	5	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Neck pain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 29 (0.00%)	2 / 11 (18.18%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Osteonecrosis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Trismus			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	6 / 29 (20.69%)	1 / 11 (9.09%)	1 / 3 (33.33%)
occurrences (all)	9	2	1
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	1 / 29 (3.45%)	2 / 11 (18.18%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Eye infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis viral			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nail infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Influenza			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 29 (0.00%)	3 / 11 (27.27%)	0 / 3 (0.00%)
occurrences (all)	0	6	0
Oral candidiasis			
subjects affected / exposed	0 / 29 (0.00%)	2 / 11 (18.18%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Sinusitis			
subjects affected / exposed	0 / 29 (0.00%)	2 / 11 (18.18%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Skin infection			
subjects affected / exposed	2 / 29 (6.90%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	5	0	0
Staphylococcal infection			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Subcutaneous abscess			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Tooth abscess			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tinea pedis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Tooth infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

Vulvovaginal candidiasis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	14 / 29 (48.28%)	6 / 11 (54.55%)	2 / 3 (66.67%)
occurrences (all)	19	10	2
Dehydration			
subjects affected / exposed	1 / 29 (3.45%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Hypercalcaemia			
subjects affected / exposed	2 / 29 (6.90%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Hyperglycaemia			
subjects affected / exposed	8 / 29 (27.59%)	2 / 11 (18.18%)	2 / 3 (66.67%)
occurrences (all)	16	6	7
Hyperlipidaemia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hyperkalaemia			
subjects affected / exposed	2 / 29 (6.90%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Hypermagnesaemia			
subjects affected / exposed	6 / 29 (20.69%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	8	2	0
Hypocalcaemia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hyperuricaemia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 11 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Hypokalaemia			

subjects affected / exposed	0 / 29 (0.00%)	0 / 11 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	2 / 29 (6.90%)	2 / 11 (18.18%)	0 / 3 (0.00%)
occurrences (all)	2	2	0
Hyponatraemia			
subjects affected / exposed	5 / 29 (17.24%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	7	1	0
Hypophosphataemia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Vitamin D deficiency			
subjects affected / exposed	0 / 29 (0.00%)	1 / 11 (9.09%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	6MG/KG		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Skin papilloma			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Haematoma			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hot flush			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pallor			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Tooth repair			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Catheter site related reaction			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Catheter site pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Crepitations			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Disease progression			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Feeling abnormal			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Influenza like illness			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Gait disturbance			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Localised oedema			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Mass			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Mucosal inflammation			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Immune system disorders			

Graft versus host disease subjects affected / exposed occurrences (all) Seasonal allergy subjects affected / exposed occurrences (all)	 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0		
Reproductive system and breast disorders Erectile dysfunction subjects affected / exposed occurrences (all) Pelvic pain subjects affected / exposed occurrences (all) Scrotal pain subjects affected / exposed occurrences (all)	 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all) Dysphonia subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all) Haemoptysis subjects affected / exposed occurrences (all) Hypoxia	 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0		

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Nasal discomfort			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pneumonitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pneumothorax			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Rhinitis allergic			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Sinus congestion			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Wheezing			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Adjustment disorder			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		

Depressed mood			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Activated partial thromboplastin time abnormal			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Bacterial test positive			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Blood glucose increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Blood phosphorus decreased			

subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Blood magnesium increased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Blood potassium decreased				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Blood sodium decreased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Blood potassium increased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Blood uric acid increased				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Blood urea increased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Body temperature				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Fungal test positive				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Gamma-glutamyltransferase increased				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Haemoglobin decreased				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	2			
International normalised ratio increased				

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Neutrophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Neutrophil count increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pulse abnormal			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Urine leukocyte esterase positive			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Weight increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Infusion related reaction			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Ligament sprain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Procedural pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Scratch			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Wound dehiscence			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Dizziness postural			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hyporeflexia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Lethargy			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Neuropathy peripheral			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Paralysis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Sinus headache			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Phantom pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Lymphopenia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Ear congestion			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Ear pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Tinnitus			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Eye disorders			

Dry eye			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Eye pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Eye pruritus			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Keratitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Miosis			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Ocular hyperaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Vision blurred			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Cheilitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Constipation			

subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Dental caries				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Diarrhoea				
subjects affected / exposed	2 / 3 (66.67%)			
occurrences (all)	3			
Dry mouth				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Dyspepsia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Dysphagia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Flatulence				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Gastrointestinal haemorrhage				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Gingival bleeding				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Haematochezia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Mouth haemorrhage				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Nausea				
subjects affected / exposed	2 / 3 (66.67%)			
occurrences (all)	3			
Oesophageal pain				

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Oral pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Sensitivity of teeth			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Tooth disorder			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Toothache			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Alopecia totalis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Blister			

subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Blood blister				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Dermal cyst				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Dermatitis contact				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Dry skin				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Eczema				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Erythema				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Nail disorder				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Hyperhidrosis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Onychoclasis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Petechiae				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Pruritus				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Rash				

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Skin irritation			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Skin discolouration			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Skin mass			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Urticaria			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Azotaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Microalbuminuria			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Renal impairment			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		

Urinary incontinence			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Endocrine disorders			
Delayed puberty			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Goitre			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypothyroidism			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Groin pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Flank pain			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Limb discomfort			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Musculoskeletal chest pain			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Musculoskeletal stiffness			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Neck pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Osteonecrosis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Trismus			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Eye infection			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Gastroenteritis viral			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Infection			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		

Nail infection				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Influenza				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Nasopharyngitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Oral candidiasis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Sinusitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Skin infection				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Staphylococcal infection				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Subcutaneous abscess				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Tooth abscess				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Tinea pedis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Tooth infection				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Urinary tract infection				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			

Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypercalcaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Hyperlipidaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hyperkalaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypermagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hyperuricaemia			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypoglycaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Vitamin D deficiency			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 July 2007	A4021010 was amended to allow for the testing of the safety and tolerability of CP-751,871 in a RP2D Extension Cohort of 12 Ewing's sarcoma patients aged 9 years or older.
12 December 2010	The protocol was amended to provide guidance on data reporting and follow-up of patients receiving CP-751,871 for more than 1 year. Also, guidance for evaluation and reportability of potential cases of liver injury has been added. Only AE, SAE and dosing information will be reported in the CRF.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The study was completed and 2 subjects in figitumumab 20 mg/kg RP2D ESFT group were transitioned to compassionate figitumumab treatment as investigators judged they were receiving benefit from the protocol therapy.

Notes: