Clinical trial results:
A Phase I Study of Monotherapy Dalotuzumab and Ridaforolimus-Dalotuzumab Combination Treatment in Paediatric Patients with Advanced Solid Tumours

Summary

EudraCT number	2011-003407-38
Trial protocol	GB FR
Global end of trial date	25 September 2013

Results information

Result version number	v1
This version publication date	26 February 2016
First version publication date	13 June 2015

Trial information

Trial identification

Sponsor protocol code	8669-062

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01431547
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill RD, Kenilworth NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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	25 September 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 September 2013
Global end of trial reached?	Yes
Global end of trial date	25 September 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This is a study of dalotuzumab given as monotherapy and in combination with ridaforolimus for pediatric participants with advanced solid tumors. This study will find the maximum tolerated dose (MTD) and collect pharmacokinetic (PK) data for dalotuzumab alone and in combination with ridaforolimus.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 February 2013
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 States: 7
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	France: 11
Worldwide total number of subjects	24
EEA total number of subjects	17

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)	12
Adolescents (12-17 years)	12
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants from age 3 to <18 years were enrolled in the dalotuzumab dose-finding cohorts; subjects of age 6 to <18 years could receive dalotuzumab-ridaforolimus combination therapy.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Dalotuzumab 900 mg/m^2

Arm description:

Participants receive dalotuzumab 900 mg/m^2, intravenously (IV) every 3 weeks

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

Dosage and administration details:

Dalotuzumab at assigned dose (based on body surface area), intravenously

Arm title	Dalotuzumab 1200 mg/m^2

Arm description:

Participants receive dalotuzumab 1200 mg/m^2, IV, every 3 weeks

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

Dosage and administration details:

Dalotuzumab at assigned dose (based on body surface area), intravenously

Arm title	Dalotuzumab 1500 mg/m^2

Arm description:

Participants receive dalotuzumab 1500 mg/m^2, IV, every 3 weeks

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

Dosage and administration details:

Dalotuzumab at assigned dose (based on body surface area), intravenously

Arm title	Dalotuzumab 900 mg/m^2 + ridaforolimus 28 mg/m^2

Arm description:

Participants receive dalotuzumab 900 mg/m^2, IV, every 3 weeks, plus ridaforolimus 28 mg/m^2 enteric-coated tablets, orally, once per day for 5 days each week

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

Dosage and administration details:

Dalotuzumab at assigned dose (based on body surface area), intravenously

Investigational medicinal product name	ridaforolimus
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ridaforolimus, enteric coated tablets. orally, once a day for 5 days per week

Number of subjects in period 1	Dalotuzumab 900 mg/m^2	Dalotuzumab 1200 mg/m^2	Dalotuzumab 1500 mg/m^2
Started	11	3	6
Completed	0	0	0
Not completed	11	3	6
Physician decision	-	-	-
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	1	-	-
Lack of efficacy	10	3	6

Number of subjects in period 1	Dalotuzumab 900 mg/m^2 + ridaforolimus 28 mg/m^2
Started	4
Completed	0
Not completed	4
Physician decision	1
Consent withdrawn by subject	1
Adverse event, non-fatal	-
Lack of efficacy	2

Baseline characteristics

Reporting groups	
Reporting group title	Dalotuzumab 900 mg/m^2
Reporting group description:	
Participants receive dalotuzumab 900 mg/m^2, intravenously (IV) every 3 weeks	
Reporting group title	Dalotuzumab 1200 mg/m^2
Reporting group description:	
Participants receive dalotuzumab 1200 mg/m^2, IV, every 3 weeks	
Reporting group title	Dalotuzumab 1500 mg/m^2
Reporting group description:	
Participants receive dalotuzumab 1500 mg/m^2, IV, every 3 weeks	
Reporting group title	Dalotuzumab 900 mg/m^2 + ridaforolimus 28 mg/m^2
Reporting group description:	
Participants receive dalotuzumab 900 mg/m^2, IV, every 3 weeks, plus ridaforolimus 28 mg/m^2 enteric-coated tablets, orally, once per day for 5 days each week	

Reporting group values	Dalotuzumab 900 mg/m^2	Dalotuzumab 1200 mg/m^2	Dalotuzumab 1500 mg/m^2
Number of subjects	11	3	6
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	6	1	4
Adolescents (12-17 years)	5	2	2
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	5	1	4
Male	6	2	2

Reporting group values	Dalotuzumab 900 mg/m^2 + ridaforolimus 28 mg/m^2	Total	
Number of subjects	4	24	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	1	12	

Adolescents (12-17 years)	3	12	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	2	12	
Male	2	12	

End points

End points reporting groups

Reporting group title	Dalotuzumab 900 mg/m^2
Reporting group description:	
Participants receive dalotuzumab 900 mg/m^2, intravenously (IV) every 3 weeks	
Reporting group title	Dalotuzumab 1200 mg/m^2
Reporting group description:	
Participants receive dalotuzumab 1200 mg/m^2, IV, every 3 weeks	
Reporting group title	Dalotuzumab 1500 mg/m^2
Reporting group description:	
Participants receive dalotuzumab 1500 mg/m^2, IV, every 3 weeks	
Reporting group title	Dalotuzumab 900 mg/m^2 + ridaforolimus 28 mg/m^2
Reporting group description:	
Participants receive dalotuzumab 900 mg/m^2, IV, every 3 weeks, plus ridaforolimus 28 mg/m^2 enteric-coated tablets, orally, once per day for 5 days each week	

Primary: Number of Participants with Dose-limiting Toxicities (DLTs)

End point title	Number of Participants with Dose-limiting Toxicities (DLTs)[1]
End point description:	
A dose-limiting toxicity is an event (medical or clinical) that results in a change in the study drug dose.	
End point type	Primary
End point timeframe:	
Up to 21 days (Cycle 1)	

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: No statistical analysis was planned for this endpoint.

End point values	Dalotuzumab 900 mg/m^2	Dalotuzumab 1200 mg/m^2	Dalotuzumab 1500 mg/m^2	Dalotuzumab 900 mg/m^2 + ridaforolimus 28 mg/m^2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	3	6	4
Units: Participants	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Concentration-Time Curve from Hour 0 to Infinity (AUC0-inf) for Dalotuzumab Alone or in Combination with Ridaforolimus

End point title	Area Under the Concentration-Time Curve from Hour 0 to Infinity (AUC0-inf) for Dalotuzumab Alone or in Combination with Ridaforolimus[2]

End point description:

AUC is a measure of the amount of drug in the body over time. The geometric mean provides the

typical value of this set of numbers by using the product of their values; the coefficient of variation provides the percent of the geometric means represented by the standard deviation and is used to compensate for the inherent differences among participants in the study.

End point type	Primary

End point timeframe:

Pre-dose and at 1, 24, 48, 168 (Day 8), and 336 hours (Day 15) post first infusion; pre-dose at Week 4 (Day 22), Week 7 (Day 43), and Weeks 13 and 19.

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: No statistical analysis was planned for this endpoint.

End point values	Dalotuzumab 900 mg/m^2	Dalotuzumab 1200 mg/m^2	Dalotuzumab 1500 mg/m^2	Dalotuzumab 900 mg/m^2 + ridaforolimus 28 mg/m^2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10[3]	3[4]	6[5]	4[6]
Units: hr*ug/mL				
geometric mean (geometric coefficient of variation)	87900 (± 61.2)	164000 (± 106)	186000 (± 79.2)	80300 (± 24.5)

Notes:

[3] - All participants taking >=1 dose of study drug(s) having required samples taken and analyzed

[4] - All participants taking >=1 dose of study drug(s) having required samples taken and analyzed

[5] - All participants taking >=1 dose of study drug(s) having required samples taken and analyzed

[6] - All participants taking >=1 dose of study drug(s) having required samples taken and analyzed

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Concentration-Time Curve from Hour 0 to Hour 24 (AUC0-24) for Ridaforolimus in Combination with Dalotuzumab

End point title	Area Under the Concentration-Time Curve from Hour 0 to Hour 24 (AUC0-24) for Ridaforolimus in Combination with Dalotuzumab[7][8]

End point description:

AUC 0-24 is a measure of the amount of drug in the body over 24 hours after the dose The geometric mean provides the typical value for the group by using the product of the AUC0-24 values; the coefficient of variation provides the percent of the geometric mean represented by the standard deviation and is used to compensate for the inherent differences among participants in the group.

End point type	Primary

End point timeframe:

Pre-dose on Days 1-5 in the first cycle of therapy and post-dose on Day 5 at 0.5, 1, 2, 4, 8, 24, and 72 hours.

Notes:

[7] - 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: No statistical analysis was planned for this endpoint.

[8] - 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: No statistical analysis was planned for this endpoint.

End point values	Dalotuzumab 900 mg/m^2 + ridaforolimus 28 mg/m^2			
Subject group type	Reporting group			
Number of subjects analysed	3[9]			
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	2350 (± 38.5)			

Notes:

[9] - One participant was excluded from the analysis due to limited samples

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse events were collected for 30 days after the last dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	Dalotuzumab 900 mg/m^2
Reporting group description:	
Participants receive dalotuzumab 900 mg/m^2, intravenously (IV) every 3 weeks	
Reporting group title	Dalotuzumab 1200 mg/m^2
Reporting group description:	
Participants receive dalotuzumab 1200 mg/m^2, IV, every 3 weeks	
Reporting group title	Dalotuzumab 1500 mg/m^2
Reporting group description:	
Participants receive dalotuzumab 1500 mg/m^2, IV, every 3 weeks	
Reporting group title	Dalotuzumab 900 mg/m^2 + ridaforolimus 28 mg/m^2
Reporting group description:	
Participants receive dalotuzumab 900 mg/m^2, IV, every 3 weeks, plus ridaforolimus 28 mg/m^2 enteric-coated tablets, orally, once per day for 5 days each week	

Serious adverse events	Dalotuzumab 900 mg/m^2	Dalotuzumab 1200 mg/m^2	Dalotuzumab 1500 mg/m^2
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 11 (63.64%)	1 / 3 (33.33%)	4 / 6 (66.67%)
number of deaths (all causes)	3	1	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	2 / 11 (18.18%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 1
Tumour pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			

Femoral neck fracture			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Neurological decompensation			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (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
Spinal cord compression			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (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 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 11 (18.18%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 11 (0.00%)	1 / 3 (33.33%)	0 / 6 (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
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			

subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Lung infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (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
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (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

Serious adverse events	Dalotuzumab 900 mg/m^2 + ridaforolimus 28 mg/m^2		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tumour pain			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Neurological decompensation			
subjects affected / exposed	0 / 4 (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 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myalgia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Lung infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 4 (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	Dalotuzumab 900 mg/m^2	Dalotuzumab 1200 mg/m^2	Dalotuzumab 1500 mg/m^2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 11 (100.00%)	3 / 3 (100.00%)	6 / 6 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Tumour associated fever			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Tumour pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hot flush			
subjects affected / exposed	2 / 11 (18.18%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Pallor			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vena cava thrombosis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Catheter site pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Chest pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	2 / 11 (18.18%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Fatigue			
subjects affected / exposed	4 / 11 (36.36%)	1 / 3 (33.33%)	3 / 6 (50.00%)
occurrences (all)	4	1	4
General physical health deterioration			

subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	4 / 11 (36.36%)	2 / 3 (66.67%)	1 / 6 (16.67%)
occurrences (all)	6	3	3
Soft tissue inflammation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Scrotal oedema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 11 (18.18%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Dyspnoea			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Epistaxis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	3 / 11 (27.27%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Orthopnoea			

subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pleural effusion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sneezing			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Tachypnoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 11 (18.18%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Insomnia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Investigations			
Alanine aminotransferase decreased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Alanine aminotransferase increased			
subjects affected / exposed	3 / 11 (27.27%)	0 / 3 (0.00%)	2 / 6 (33.33%)
occurrences (all)	4	0	2
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 11 (18.18%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	3
Bilirubin conjugated increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood albumin decreased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			

subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blood bilirubin increased			
subjects affected / exposed	2 / 11 (18.18%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Blood calcium decreased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood cholesterol increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Blood creatinine increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Blood glucose decreased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blood magnesium decreased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Blood potassium decreased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blood sodium decreased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blood triglycerides increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	3
Blood uric acid increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase			

increased			
subjects affected / exposed	3 / 11 (27.27%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	5	0	1
Haemoglobin decreased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Haemoglobin increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
High density lipoprotein increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Low density lipoprotein increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	3 / 11 (27.27%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Neutrophil count decreased			
subjects affected / exposed	2 / 11 (18.18%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences (all)	3	1	1
Platelet count decreased			
subjects affected / exposed	3 / 11 (27.27%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Protein total decreased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Weight increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	3 / 11 (27.27%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences (all)	10	1	1

Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Head injury			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Infusion related reaction			
subjects affected / exposed	3 / 11 (27.27%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	3	0	1
Procedural pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Scratch			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Cyanosis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nervous system disorders			
Cerebellar syndrome			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	4 / 11 (36.36%)	1 / 3 (33.33%)	2 / 6 (33.33%)
occurrences (all)	13	1	4

Hyperaesthesia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyporeflexia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Lethargy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Slow speech			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 11 (18.18%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences (all)	5	1	1
Neutropenia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Ear swelling			
subjects affected / exposed	0 / 11 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Otorrhoea			
subjects affected / exposed	0 / 11 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Eye disorders			

Diplopia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Erythema of eyelid			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Lacrimation increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Photophobia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 11 (18.18%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences (all)	4	1	1
Abdominal pain upper			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Anal fissure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Ascites			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chapped lips			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Constipation			

subjects affected / exposed	4 / 11 (36.36%)	1 / 3 (33.33%)	3 / 6 (50.00%)
occurrences (all)	5	1	3
Diarrhoea			
subjects affected / exposed	3 / 11 (27.27%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Dry mouth			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hyoaesthesia oral			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	3 / 11 (27.27%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences (all)	5	1	2
Oral pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Salivary hypersecretion			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	2 / 11 (18.18%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Vomiting			

subjects affected / exposed	3 / 11 (27.27%)	2 / 3 (66.67%)	3 / 6 (50.00%)
occurrences (all)	8	2	5
Hepatobiliary disorders			
Hepatic pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperbilirubinaemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	2 / 11 (18.18%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Dry skin			
subjects affected / exposed	0 / 11 (0.00%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences (all)	0	2	1
Erythema			
subjects affected / exposed	0 / 11 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Palmar erythema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Petechiae			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	2 / 11 (18.18%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Rash			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Rash macular			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Rash papular			

subjects affected / exposed	0 / 11 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Rash pruritic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Swelling face			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Cystitis noninfective			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 11 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Incontinence			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Proteinuria			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Back pain			
subjects affected / exposed	3 / 11 (27.27%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Bone pain			

subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Myalgia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Pain in extremity			
subjects affected / exposed	1 / 11 (9.09%)	2 / 3 (66.67%)	0 / 6 (0.00%)
occurrences (all)	2	2	0
Infections and infestations			
Ear infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	2
Lower respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Lung infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0

Nasopharyngitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Oral candidiasis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Rhinitis			
subjects affected / exposed	2 / 11 (18.18%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Sphingomonas paucimobilis infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Staphylococcal infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	3 / 11 (27.27%)	1 / 3 (33.33%)	2 / 6 (33.33%)
occurrences (all)	3	1	3
Dehydration			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypercalcaemia			
subjects affected / exposed	2 / 11 (18.18%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Hyperglycaemia			
subjects affected / exposed	3 / 11 (27.27%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	7	0	4
Hypermagnesaemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Hypernatraemia			

subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hyperphosphataemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Hypertriglyceridaemia			
subjects affected / exposed	2 / 11 (18.18%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	3	0	1
Hypoalbuminaemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Hypocalcaemia			
subjects affected / exposed	3 / 11 (27.27%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	3	0	1
Hypokalaemia			
subjects affected / exposed	2 / 11 (18.18%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	10	0	1
Hypomagnesaemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Hyponatraemia			
subjects affected / exposed	4 / 11 (36.36%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences (all)	7	1	4
Hypophosphataemia			
subjects affected / exposed	2 / 11 (18.18%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	3	0	3

Non-serious adverse events	Dalotuzumab 900 mg/m^2 + ridaforolimus 28 mg/m^2		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour associated fever			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Tumour pain			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hot flush			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pallor			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Vena cava thrombosis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Catheter site pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	3		
Chills			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	2		
General physical health deterioration			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Malaise			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	3		
Pyrexia			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	3		
Soft tissue inflammation			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Scrotal oedema			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Epistaxis			
subjects affected / exposed	3 / 4 (75.00%)		
occurrences (all)	4		
Nasal congestion			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Orthopnoea			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pleural effusion			

subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Sneezing			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Tachypnoea			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	2		
Insomnia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Investigations			
Alanine aminotransferase decreased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Alanine aminotransferase increased			
subjects affected / exposed	3 / 4 (75.00%)		
occurrences (all)	4		
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	3		
Bilirubin conjugated increased			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Blood albumin decreased			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Blood bilirubin increased			

subjects affected / exposed	2 / 4 (50.00%)			
occurrences (all)	5			
Blood calcium decreased				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences (all)	1			
Blood cholesterol increased				
subjects affected / exposed	2 / 4 (50.00%)			
occurrences (all)	2			
Blood creatinine increased				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences (all)	1			
Blood glucose decreased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Blood magnesium decreased				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences (all)	2			
Blood phosphorus decreased				
subjects affected / exposed	2 / 4 (50.00%)			
occurrences (all)	2			
Blood potassium decreased				
subjects affected / exposed	3 / 4 (75.00%)			
occurrences (all)	4			
Blood sodium decreased				
subjects affected / exposed	2 / 4 (50.00%)			
occurrences (all)	4			
Blood triglycerides increased				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences (all)	2			
Blood uric acid increased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Gamma-glutamyltransferase increased				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences (all)	1			

Haemoglobin decreased subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 4		
Haemoglobin increased subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
High density lipoprotein increased subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Low density lipoprotein increased subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Lymphocyte count decreased subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 6		
Neutrophil count decreased subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Platelet count decreased subjects affected / exposed occurrences (all)	4 / 4 (100.00%) 8		
Protein total decreased subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Weight decreased subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 2		
Weight increased subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 2		
White blood cell count decreased subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 3		
Injury, poisoning and procedural complications			

Arthropod bite			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Fall			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Head injury			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Infusion related reaction			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Procedural pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Scratch			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Cardiac disorders			
Cyanosis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Tachycardia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	2		
Nervous system disorders			
Cerebellar syndrome			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	6		
Hyperaesthesia			

subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Hyporeflexia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Lethargy subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Paraesthesia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Slow speech subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Neutropenia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Ear and labyrinth disorders			
Ear pain subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Ear swelling subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Otorrhoea subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Eye disorders			

Diplopia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Erythema of eyelid				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Lacrimation increased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Ocular hyperaemia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Photophobia				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences (all)	2			
Vision blurred				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	2 / 4 (50.00%)			
occurrences (all)	4			
Abdominal pain upper				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences (all)	1			
Anal fissure				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences (all)	1			
Ascites				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences (all)	1			
Chapped lips				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Constipation				

subjects affected / exposed	4 / 4 (100.00%)			
occurrences (all)	8			
Diarrhoea				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences (all)	1			
Dry mouth				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences (all)	2			
Flatulence				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences (all)	1			
Hyoaesthesia oral				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Nausea				
subjects affected / exposed	3 / 4 (75.00%)			
occurrences (all)	3			
Oral pain				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences (all)	1			
Proctalgia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Rectal haemorrhage				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Salivary hypersecretion				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Stomatitis				
subjects affected / exposed	4 / 4 (100.00%)			
occurrences (all)	6			
Toothache				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Vomiting				

subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	6		
Hepatobiliary disorders			
Hepatic pain			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Hyperbilirubinaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Erythema			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Palmar erythema			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Petechiae			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	2		
Pruritus			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Rash macular			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Rash papular			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Rash pruritic			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Skin lesion			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Swelling face			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Cystitis noninfective			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	2		
Dysuria			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Haematuria			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Incontinence			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Proteinuria			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	5		
Back pain			
subjects affected / exposed	3 / 4 (75.00%)		
occurrences (all)	4		
Bone pain			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Muscular weakness			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Musculoskeletal chest pain			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	3		
Musculoskeletal pain			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	5		
Myalgia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	4		
Infections and infestations			
Ear infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Herpes zoster			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Lower respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Lung infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		

Nasopharyngitis subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 2			
Oral candidiasis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0			
Rhinitis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0			
Sphingomonas paucimobilis infection subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0			
Staphylococcal infection subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0			
Metabolism and nutrition disorders Cachexia subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1			
Decreased appetite subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 2			
Dehydration subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0			
Hypercalcaemia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0			
Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0			
Hypermagnesaemia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0			
Hypernatraemia				

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hyperphosphataemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypertriglyceridaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypoalbuminaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypocalcaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypomagnesaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypophosphataemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported