Clinical trial results:
A Phase I Study of Ridaforolimus in Paediatric Patients with Advanced Solid Tumours

Summary

EudraCT number	2011-000729-55
Trial protocol	GB FR Outside EU/EEA
Global end of trial date	

Results information

Result version number	v1
This version publication date	26 February 2016
First version publication date	19 July 2015

Trial information

Trial identification

Sponsor protocol code	MK-8669-056

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01431534
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. , Clinical Trials Disclosure, Merck Sharp & Dohme Corp. , ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp. , Clinical Trials Disclosure, Merck Sharp & Dohme Corp. , ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000458-PIP01-08
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	Interim
Date of interim/final analysis	30 April 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 August 2013
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the recommended dose of ridaforolimus for participants with advanced solid tumors by measuring:
• The number of participants experiencing dose-limiting toxicities (DLTs) while on different doses of ridaforolimus
• The amount of ridaforolimus in the blood over 24 hours after a dose is given to find the correct therapeutic dose

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	30 January 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	United States: 4
Worldwide total number of subjects	20
EEA total number of subjects	16

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)	7
Adolescents (12-17 years)	13
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:

This study enrolled children from the ages of 6 to <18 years with advanced solid tumors including lymphoma and tumors of the central nervous system who met the study inclusion/exclusion criteria

Period 1

Period 1 title	Treatment Phase
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Ridaforolimus 22 mg/m^2

Arm description:

Participants receive ridaforolimus 22 mg/m^2, orally, 10 mg enteric-coated tablet once daily (QD) for 5 days with 2 days of rest each week (QD x5/week), in 28-day cycles

Arm type	Experimental
Investigational medicinal product name	Ridaforolimus
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

22 mg/m^2, orally, 10 mg enteric-coated tablet QD x 5/week, in 28-day cycles

Arm title	Ridaforolimus 28mg/m^2

Arm description:

Participants receive ridaforolimus 28mg/m^2, orally, 10 mg enteric-coated tablet QD x 5/week, in 28-day cycles

Arm type	Experimental
Investigational medicinal product name	Ridaforolimus
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

28 mg/m^2, orally, 10 mg enteric-coated tablet QD x 5/week, in 28-day cycles

Arm title	Ridaforolimus 33 mg/m^2

Arm description:

Participants receive ridaforolimus 33 mg/m^2, orally, 10 mg enteric-coated tablet QD x 5/week, in 28-day cycles

Arm type	Experimental
Investigational medicinal product name	Ridaforolimus
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

33 mg/m^2, orally, 10 mg enteric-coated tablet QD x 5/week, in 28-day cycles

Number of subjects in period 1	Ridaforolimus 22 mg/m^2	Ridaforolimus 28mg/m^2	Ridaforolimus 33 mg/m^2
Started	4	3	13
Completed	0	0	2
Not completed	4	3	11
Adverse event, non-fatal	-	-	1
Lack of efficacy	4	3	10

Period 2

Period 2 title	Extension Phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Ridaforolimus 33 mg/m^2

Arm description:

Participants receive ridaforolimus 33 mg/m^2, orally, 10 mg enteric-coated tablet QD x 5/week, in 28-day cycles; this population comprises all participants who did not have disease progression, adequately tolerated therapy, and continued to meet study eligibility criteria for 6 months after the trial's enrollment period was complete.

Arm type	Experimental
Investigational medicinal product name	Ridaforolimus
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

33 mg/m^2, orally, 10 mg enteric-coated tablet QD x 5/week, in 28-day cycles

Number of subjects in period 2	Ridaforolimus 33 mg/m^2
Started	2
Completed	0
Not completed	2
Participant still on treatment	2

Baseline characteristics

Reporting groups	
Reporting group title	Ridaforolimus 22 mg/m^2
Reporting group description:	
Participants receive ridaforolimus 22 mg/m^2, orally, 10 mg enteric-coated tablet once daily (QD) for 5 days with 2 days of rest each week (QD x5/week), in 28-day cycles	
Reporting group title	Ridaforolimus 28mg/m^2
Reporting group description:	
Participants receive ridaforolimus 28mg/m^2, orally, 10 mg enteric-coated tablet QD x 5/week, in 28-day cycles	
Reporting group title	Ridaforolimus 33 mg/m^2
Reporting group description:	
Participants receive ridaforolimus 33 mg/m^2, orally, 10 mg enteric-coated tablet QD x 5/week, in 28-day cycles	

Reporting group values	Ridaforolimus 22 mg/m^2	Ridaforolimus 28mg/m^2	Ridaforolimus 33 mg/m^2
Number of subjects	4	3	13
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)	1	0	6
Adolescents (12-17 years)	3	3	7
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	2	2	8
Male	2	1	5

Reporting group values	Total		
Number of subjects	20		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	7		
Adolescents (12-17 years)	13		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		

Gender categorical Units: Subjects			
Female	12		
Male	8		

End points

End points reporting groups

Reporting group title	Ridaforolimus 22 mg/m^2
Reporting group description:	
Participants receive ridaforolimus 22 mg/m^2, orally, 10 mg enteric-coated tablet once daily (QD) for 5 days with 2 days of rest each week (QD x5/week), in 28-day cycles	
Reporting group title	Ridaforolimus 28mg/m^2
Reporting group description:	
Participants receive ridaforolimus 28mg/m^2, orally, 10 mg enteric-coated tablet QD x 5/week, in 28-day cycles	
Reporting group title	Ridaforolimus 33 mg/m^2
Reporting group description:	
Participants receive ridaforolimus 33 mg/m^2, orally, 10 mg enteric-coated tablet QD x 5/week, in 28-day cycles	
Reporting group title	Ridaforolimus 33 mg/m^2
Reporting group description:	
Participants receive ridaforolimus 33 mg/m^2, orally, 10 mg enteric-coated tablet QD x 5/week, in 28-day cycles; this population comprises all participants who did not have disease progression, adequately tolerated therapy, and continued to meet study eligibility criteria for 6 months after the trial's enrollment period was complete.	

Primary: Number of subjects experiencing a dose-limiting toxicity (DLT)

End point title	Number of subjects experiencing a dose-limiting toxicity
End point description:	
A dose-limiting toxicity is an event (a medical or clinical) experienced by a participant that results in stopping the drug treatment or lowering the dose.	
End point type	Primary
End point timeframe:	
Cycle 1, up to 28 days	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this endpoint.

End point values	Ridaforolimus 22 mg/m^2	Ridaforolimus 28mg/m^2	Ridaforolimus 33 mg/m^2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	3	13	
Units: subjects	0	0	1	

Statistical analyses

No statistical analyses for this end point

Primary: Area under the concentration curve from Hour 0 to Hour 24 (AUC0-24) for ridaforolimus

End point title	Area under the concentration curve from Hour 0 to Hour 24 (AUC0-24) for ridaforolimus[2]

End point description:

AUC0-24 is a measure of the amount of drug in the blood over time. For this endpoint, only participants who received all five drug doses in the first week of Cycle 1 of therapy were included.

End point type	Primary

End point timeframe:

Pre-dose on Days 1-4, and pre-dose and at 0.5, 1, 2, 4, 8, 24, and 72 hours post-dose on Day 5

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	Ridaforolimus 22 mg/m^2	Ridaforolimus 28mg/m^2	Ridaforolimus 33 mg/m^2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	3	11	
Units: hr*ng/mL				
arithmetic mean (standard deviation)	1390 (± 437)	2420 (± 777)	2370 (± 671)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to 4 weeks after last dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	Ridaforolimus 22 mg/m^2
Reporting group description: Participants receive ridaforolimus 22 mg/m^2, orally, 10 mg enteric-coated tablet QD x 5/week, in 28-day cycles	
Reporting group title	Ridaforolimus 28mg/m^2
Reporting group description: Participants receive ridaforolimus 28mg/m^2, orally, 10 mg enteric-coated tablet QD x 5/week, in 28-day cycles	
Reporting group title	Ridaforolimus 33 mg/m^2
Reporting group description: Participants receive ridaforolimus 33 mg/m^2, orally, 10 mg enteric-coated tablet QD x 5/week, in 28-day cycles	

Serious adverse events	Ridaforolimus 22 mg/m^2	Ridaforolimus 28mg/m^2	Ridaforolimus 33 mg/m^2
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 4 (75.00%)	2 / 3 (66.67%)	7 / 13 (53.85%)
number of deaths (all causes)	1	1	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm progression			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Nervous system disorders			
Convulsion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			

subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 13 (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
Neurological symptom			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Partial seizure			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (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
Gastrointestinal disorders			
Gastric perforation			
subjects affected / exposed	0 / 4 (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 / 1
Proctalgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 4 (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
Pneumothorax			
subjects affected / exposed	0 / 4 (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

Infections and infestations			
Device related sepsis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (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
Herpes virus infection			
subjects affected / exposed	0 / 4 (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
Lung infection			
subjects affected / exposed	0 / 4 (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
Oral herpes			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (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
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhinovirus infection			
subjects affected / exposed	0 / 4 (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
Tracheitis			
subjects affected / exposed	0 / 4 (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
Viral infection			
subjects affected / exposed	0 / 4 (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

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

Non-serious adverse events	Ridaforolimus 22 mg/m^2	Ridaforolimus 28mg/m^2	Ridaforolimus 33 mg/m^2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (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 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Catheter site pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Chest pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	1 / 13 (7.69%)
occurrences (all)	0	2	1
Chills			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Fatigue			
subjects affected / exposed	4 / 4 (100.00%)	3 / 3 (100.00%)	7 / 13 (53.85%)
occurrences (all)	4	3	8
Gait disturbance			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Local swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1

Oedema peripheral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	3 / 13 (23.08%)
occurrences (all)	0	0	3
Pyrexia			
subjects affected / exposed	3 / 4 (75.00%)	1 / 3 (33.33%)	4 / 13 (30.77%)
occurrences (all)	3	2	4
Thrombus in device			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Drug hypersensitivity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	6 / 13 (46.15%)
occurrences (all)	2	1	8
Dysphonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	3 / 13 (23.08%)
occurrences (all)	0	1	3
Epistaxis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	3 / 13 (23.08%)
occurrences (all)	0	0	3
Haemoptysis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Hiccups			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Increased upper airway secretion			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Laryngeal inflammation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Nasal dryness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	3 / 13 (23.08%)
occurrences (all)	0	0	5
Pleural effusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Respiratory distress			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Sputum discoloured			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Psychiatric disorders			
Agitation			
subjects affected / exposed	2 / 4 (50.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Anxiety			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	2 / 13 (15.38%)
occurrences (all)	1	0	2
Confusional state			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1

Depression			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences (all)	1	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	9 / 13 (69.23%)
occurrences (all)	4	1	15
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 4 (25.00%)	2 / 3 (66.67%)	8 / 13 (61.54%)
occurrences (all)	2	2	15
Blood albumin decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	2 / 13 (15.38%)
occurrences (all)	1	1	2
Blood bilirubin increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	4 / 13 (30.77%)
occurrences (all)	1	0	5
Blood calcium decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	3 / 13 (23.08%)
occurrences (all)	0	0	4
Blood chloride decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Blood cholesterol increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	5 / 13 (38.46%)
occurrences (all)	0	0	8
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Blood creatinine increased			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	6 / 13 (46.15%)
occurrences (all)	0	0	6
Blood glucose decreased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Blood glucose increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Blood magnesium decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	2
Blood magnesium increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Blood phosphorus decreased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	4 / 13 (30.77%)
occurrences (all)	1	0	8
Blood phosphorus increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Blood potassium decreased			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	1 / 13 (7.69%)
occurrences (all)	6	1	3
Blood selenium increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Blood sodium decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Blood triglycerides increased			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	4 / 13 (30.77%)
occurrences (all)	2	2	5
C-reactive protein increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	2
Haemoglobin decreased			

subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	2 / 13 (15.38%)
occurrences (all)	4	2	6
International normalised ratio decreased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	4 / 13 (30.77%)
occurrences (all)	5	0	5
Neutrophil count decreased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	2 / 13 (15.38%)
occurrences (all)	4	0	2
Platelet count decreased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	10 / 13 (76.92%)
occurrences (all)	3	0	17
Reticulocyte count decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	4 / 13 (30.77%)
occurrences (all)	0	0	4
White blood cell count decreased			
subjects affected / exposed	1 / 4 (25.00%)	2 / 3 (66.67%)	4 / 13 (30.77%)
occurrences (all)	5	3	9
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Animal bite			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Procedural pain			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	2
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Wolff-Parkinson-White syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Ataxia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Dysarthria			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	3 / 13 (23.08%)
occurrences (all)	0	0	3
Extrapyramidal disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	3 / 4 (75.00%)	1 / 3 (33.33%)	6 / 13 (46.15%)
occurrences (all)	6	2	11
Hyporeflexia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Paraparesis			

subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Tremor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
V11th nerve paralysis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	2
Dizziness			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences (all)	2	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	3 / 13 (23.08%)
occurrences (all)	2	0	6
Leukopenia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Lymphopenia			
subjects affected / exposed	2 / 4 (50.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Neutropenia			
subjects affected / exposed	2 / 4 (50.00%)	1 / 3 (33.33%)	3 / 13 (23.08%)
occurrences (all)	4	1	6
Thrombocytopenia			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences (all)	1	1	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Eyelid ptosis			

subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Mydriasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Photophobia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	2 / 13 (15.38%)
occurrences (all)	0	1	2
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	2 / 4 (50.00%)	1 / 3 (33.33%)	2 / 13 (15.38%)
occurrences (all)	4	1	2
Aphthous stomatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	1 / 4 (25.00%)	2 / 3 (66.67%)	6 / 13 (46.15%)
occurrences (all)	1	2	7
Diarrhoea			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	6 / 13 (46.15%)
occurrences (all)	2	0	11
Dry mouth			
subjects affected / exposed	2 / 4 (50.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	3	0	1
Dyspepsia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Gastroesophageal reflux disease			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Hypoaesthesia oral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1

Lip dry			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Lip Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	4 / 4 (100.00%)	2 / 3 (66.67%)	8 / 13 (61.54%)
occurrences (all)	6	2	11
Odynophagia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Oral dysaesthesia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Oral pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Salivary hypersecretion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Stomatitis			
subjects affected / exposed	2 / 4 (50.00%)	3 / 3 (100.00%)	10 / 13 (76.92%)
occurrences (all)	3	4	18
Toothache			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	3
Vomiting			
subjects affected / exposed	2 / 4 (50.00%)	1 / 3 (33.33%)	7 / 13 (53.85%)
occurrences (all)	12	1	10
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 4 (25.00%)	2 / 3 (66.67%)	5 / 13 (38.46%)
occurrences (all)	1	2	6
Skin and subcutaneous tissue disorders			

Decubitus ulcer			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Dry skin			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Eczema			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Hair texture abnormal			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Petechiae			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Pruritus			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	1 / 13 (7.69%)
occurrences (all)	1	1	1
Rash maculo-papular			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Skin lesion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Skin striae			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Enuresis			

subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Haematuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Haemorrhage urinary tract			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Micturition urgency			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Pollakiuria			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Proteinuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	3 / 13 (23.08%)
occurrences (all)	0	0	3
Urinary hesitation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Urinary incontinence			
subjects affected / exposed	2 / 4 (50.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	2	0	1
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 4 (25.00%)	3 / 3 (100.00%)	2 / 13 (15.38%)
occurrences (all)	1	3	2
Back pain			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	2 / 13 (15.38%)
occurrences (all)	1	1	2
Bone pain			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Groin pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Joint swelling			
subjects affected / exposed	0 / 4 (0.00%)	2 / 3 (66.67%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Muscle spasms			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain			
subjects affected / exposed	2 / 4 (50.00%)	2 / 3 (66.67%)	3 / 13 (23.08%)
occurrences (all)	5	2	3
Myalgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Myopathy			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Osteonecrosis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	4 / 13 (30.77%)
occurrences (all)	4	0	6
Pain in jaw			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Infections and infestations			
Catheter site infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0

Ear infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Genital herpes			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Impetigo			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Oral herpes			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	2
Otitis media			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Pleural infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Skin infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Staphylococcal skin infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Tracheitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1

Upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Varicella			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Vulvitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Wound infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 4 (50.00%)	2 / 3 (66.67%)	6 / 13 (46.15%)
occurrences (all)	2	2	7
Dehydration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Fluid retention			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Hypercholesterolemia			
subjects affected / exposed	2 / 4 (50.00%)	1 / 3 (33.33%)	1 / 13 (7.69%)
occurrences (all)	3	2	1
Hyperglycaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	4 / 13 (30.77%)
occurrences (all)	1	0	7
Hypernatraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	2
Hypertriglyceridaemia			

subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	4 / 13 (30.77%)
occurrences (all)	1	0	4
Hypoalbuminaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	2 / 13 (15.38%)
occurrences (all)	1	0	4
Hypocalcaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	3 / 13 (23.08%)
occurrences (all)	1	0	6
Hypoglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Hypokalaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	3 / 13 (23.08%)
occurrences (all)	2	0	9
Hypomagnesaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	5
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	2
Hypophosphataemia			
subjects affected / exposed	2 / 4 (50.00%)	1 / 3 (33.33%)	1 / 13 (7.69%)
occurrences (all)	3	2	6
Iron deficiency			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1

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

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

At the time of database lock (17-Dec-2013), 2 subjects were still receiving treatment.

Notes: