



## 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	v2
This version publication date	03 March 2016
First version publication date	19 July 2015
Version creation reason	

#### Trial information

##### Trial identification

Sponsor protocol code	8669-056
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##### 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., 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)	Yes
EMA paediatric investigation plan number(s)	EMA-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:

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**Results analysis stage**

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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

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Notes:

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**General information about the trial**

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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
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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.

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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

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Notes:

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**Population of trial subjects**

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**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

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Notes:

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**Subjects enrolled per age group**

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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

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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
<b>Arm title</b>	Ridaforolimus 22 mg/m <sup>2</sup>

Arm description:

Participants receive ridaforolimus 22 mg/m<sup>2</sup>, 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<sup>2</sup>, orally, 10 mg enteric-coated tablet QD x 5/week, in 28-day cycles

<b>Arm title</b>	Ridaforolimus 28mg/m <sup>2</sup>
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Arm description:

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

<b>Arm title</b>	Ridaforolimus 33 mg/m <sup>2</sup>
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Arm description:

Participants receive ridaforolimus 33 mg/m<sup>2</sup>, 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

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**Dosage and administration details:**

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

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

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**Period 2**

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

**Arms**

<b>Arm title</b>	Ridaforolimus 33 mg/m <sup>2</sup>
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**Arm description:**

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

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

## Baseline characteristics

### Reporting groups

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

Reporting group values	Ridaforolimus 22 mg/m <sup>2</sup>	Ridaforolimus 28mg/m <sup>2</sup>	Ridaforolimus 33 mg/m <sup>2</sup>
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 <sup>2</sup>
Reporting group description: Participants receive ridaforolimus 22 mg/m <sup>2</sup> , 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 <sup>2</sup>
Reporting group description: Participants receive ridaforolimus 28mg/m <sup>2</sup> , orally, 10 mg enteric-coated tablet QD x 5/week, in 28-day cycles	
Reporting group title	Ridaforolimus 33 mg/m <sup>2</sup>
Reporting group description: Participants receive ridaforolimus 33 mg/m <sup>2</sup> , orally, 10 mg enteric-coated tablet QD x 5/week, in 28-day cycles	
Reporting group title	Ridaforolimus 33 mg/m <sup>2</sup>
Reporting group description: Participants receive ridaforolimus 33 mg/m <sup>2</sup> , 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 <sup>2</sup>	Ridaforolimus 28mg/m <sup>2</sup>	Ridaforolimus 33 mg/m <sup>2</sup>	
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 <sup>[2]</sup>
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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.

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End point type	Primary
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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

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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 <sup>2</sup>	Ridaforolimus 28mg/m <sup>2</sup>	Ridaforolimus 33 mg/m <sup>2</sup>	
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

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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
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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### Reporting groups

Reporting group title	Ridaforolimus 22 mg/m <sup>2</sup>
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Reporting group description:

Participants receive ridaforolimus 22 mg/m<sup>2</sup>, orally, 10 mg enteric-coated tablet QD x 5/week, in 28-day cycles

Reporting group title	Ridaforolimus 28mg/m <sup>2</sup>
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Reporting group description:

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

Reporting group title	Ridaforolimus 33 mg/m <sup>2</sup>
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Reporting group description:

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

Serious adverse events	Ridaforolimus 22 mg/m <sup>2</sup>	Ridaforolimus 28mg/m <sup>2</sup>	Ridaforolimus 33 mg/m <sup>2</sup>
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	0	0	0
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 / 1	0 / 0	0 / 0
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 occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 4 (25.00%) 0 / 1 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 13 (0.00%) 0 / 0 0 / 0
Herpes virus infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 4 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0	1 / 13 (7.69%) 0 / 1 0 / 0
Lung infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 4 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0	1 / 13 (7.69%) 0 / 1 0 / 0
Oral herpes subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 4 (25.00%) 1 / 1 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 13 (0.00%) 0 / 0 0 / 0
Pneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 4 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0	1 / 13 (7.69%) 0 / 1 0 / 0
Rhinovirus infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 4 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0	1 / 13 (7.69%) 0 / 1 0 / 0
Tracheitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 4 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0	1 / 13 (7.69%) 0 / 1 0 / 0
Viral infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 4 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0	1 / 13 (7.69%) 0 / 1 0 / 0

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

<b>Non-serious adverse events</b>	Ridaforolimus 22 mg/m <sup>2</sup>	Ridaforolimus 28mg/m <sup>2</sup>	Ridaforolimus 33 mg/m <sup>2</sup>
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 occurrences (all)	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0	3 / 13 (23.08%) 3
Pyrexia subjects affected / exposed occurrences (all)	3 / 4 (75.00%) 3	1 / 3 (33.33%) 2	4 / 13 (30.77%) 4
Thrombus in device subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0	1 / 13 (7.69%) 1
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0	1 / 13 (7.69%) 1
Drug hypersensitivity subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0	1 / 13 (7.69%) 1
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 2	1 / 3 (33.33%) 1	6 / 13 (46.15%) 8
Dysphonia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0	1 / 13 (7.69%) 1
Dyspnoea subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 3 (33.33%) 1	3 / 13 (23.08%) 3
Epistaxis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0	3 / 13 (23.08%) 3
Haemoptysis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0	1 / 13 (7.69%) 1
Hiccups subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0	1 / 13 (7.69%) 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
Gamma-glutamyltransferase			

increased			
subjects affected / exposed	1 / 4 (25.00%)	2 / 3 (66.67%)	5 / 13 (38.46%)
occurrences (all)	1	2	6
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
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 occurrences (all)	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0	1 / 13 (7.69%) 1
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 3 (0.00%) 0	1 / 13 (7.69%) 1
Varicella subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0	1 / 13 (7.69%) 1
Vulvitis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0	1 / 13 (7.69%) 1
Wound infection subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0	1 / 13 (7.69%) 1
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 2	2 / 3 (66.67%) 2	6 / 13 (46.15%) 7
Dehydration subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0	1 / 13 (7.69%) 1
Fluid retention subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0	1 / 13 (7.69%) 1
Hypercholesterolemia subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 3	1 / 3 (33.33%) 2	1 / 13 (7.69%) 1
Hyperglycaemia subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 3 (0.00%) 0	4 / 13 (30.77%) 7
Hypernatraemia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0	1 / 13 (7.69%) 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

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### 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.
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Notes: