Clinical trial results:
A Phase I/II Safety and Exploratory Pharmacodynamic Study of Intravenous Temsirolimus (CCI-779) in Pediatric Subjects with Relapsed/Refractory Solid Tumors

Summary

EudraCT number	2007-000371-42
Trial protocol	FR DE PL
Global end of trial date	04 January 2012

Results information

Result version number	v1
This version publication date	16 March 2016
First version publication date	29 July 2015

Trial information

Trial identification

Sponsor protocol code	3066K1-139

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00106353
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer Inc., Pfizer ClinicalTrials.gov Call Center, 00 1-800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer Inc., Pfizer ClinicalTrials.gov Call Center, 00 1-800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 July 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 January 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Part 1:
Primary Objective - To evaluate the safety of intravenously (IV) temsirolimus given once weekly to children with solid tumors with disease that is recurrent or refractory to standard therapy or for whom standard therapy is not available.

Part 2:
Primary objective - To obtain preliminary information on the anti-tumor activity of IV temsirolimus in children with relapsed/refractory neuroblastoma, high-grade gliomas, and rhabdomyosarcoma. Anti-tumor activity will be assessed by determining the percentage of subjects exhibiting objective response (Confirmed response [CR] + Partial response [PR]) within 12 weeks.

Protection of trial subjects:

The study was in compliance with with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 January 2005
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Poland: 3
Country: Number of subjects enrolled	Russian Federation: 3
Country: Number of subjects enrolled	United States: 62
Worldwide total number of subjects	71
EEA total number of subjects	6

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)	2
Children (2-11 years)	41
Adolescents (12-17 years)	16
Adults (18-64 years)	12
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was conducted in 7 countries between 26 January 2005 and 4 January 2012.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Temsirolimus 10 mg/m^2: Part 1

Arm description:

Temsirolimus was administered intravenously over 60 minutes infusion.

Arm type	Experimental
Investigational medicinal product name	Temsirolimus
Investigational medicinal product code	CCI-779
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

10 milligram per square meter (mg/m^2) was administered intravenously once weekly.

Arm title	Temsirolimus 25 mg/m^2: Part 1

Arm description:

Temsirolimus was administered intravenously over 60 minutes infusion.

Arm type	Experimental
Investigational medicinal product name	Temsirolimus
Investigational medicinal product code	CCI-779
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

25 mg/m^2 was administered intravenously once weekly.

Arm title	Temsirolimus 75 mg/m^2: Part 1

Arm description:

Temsirolimus was administered intravenously over 60 minutes infusion.

Arm type	Experimental
Investigational medicinal product name	Temsirolimus
Investigational medicinal product code	CCI-779
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

75 mg/m^2 was administered intravenously once weekly.

Arm title	Temsirolimus 150 mg/m^2: Part 1

Arm description:

Temsirolimus was administered intravenously over 60 minutes infusion.

Arm type	Experimental
Investigational medicinal product name	Temsirolimus
Investigational medicinal product code	CCI-779
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

150 mg/m^2 was administered intravenously once weekly.

Arm title	High-grade Glioma: Part 2

Arm description:

Temsirolimus was administered intravenously to subjects with high-grade glioma over 60 minutes infusion.

Arm type	Experimental
Investigational medicinal product name	Temsirolimus
Investigational medicinal product code	CCI-779
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

75 mg/m^2 was administered intravenously once weekly.

Arm title	Neuroblastoma: Part 2

Arm description:

Temsirolimus was administered intravenously to subjects with neuroblatoma over 60 minutes infusion.

Arm type	Experimental
Investigational medicinal product name	Temsirolimus
Investigational medicinal product code	CCI-779
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

75 mg/m^2 was administered intravenously once weekly.

Arm title	Rhabdomyosarcoma: Part 2

Arm description:

Temsirolimus was administered intravenously to subjects with rhabdomyosarcoma over 60 minutes infusion.

Arm type	Experimental
Investigational medicinal product name	Temsirolimus
Investigational medicinal product code	CCI-779
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

75 mg/m^2 was administered intravenously once weekly.

Number of subjects in period 1	Temsirolimus 10 mg/m^2: Part 1	Temsirolimus 25 mg/m^2: Part 1	Temsirolimus 75 mg/m^2: Part 1
Started	4	5	3
Completed	0	0	0
Not completed	4	5	3
Entered follow-up phase	1	1	-
Consent withdrawn by subject	-	-	1
Physician decision	-	-	-
Disease progression	3	4	1
Symptomatic deterioration	-	-	1
Death	-	-	-
Adverse event	-	-	-
Unspecified	-	-	-

Number of subjects in period 1	Temsirolimus 150 mg/m^2: Part 1	High-grade Glioma: Part 2	Neuroblastoma: Part 2
Started	7	17	19
Completed	0	1	1
Not completed	7	16	18
Entered follow-up phase	1	-	-
Consent withdrawn by subject	2	1	-
Physician decision	-	-	1
Disease progression	3	8	14
Symptomatic deterioration	-	3	-
Death	-	3	-
Adverse event	1	-	2
Unspecified	-	1	1

Number of subjects in period 1	Rhabdomyosarcoma: Part 2
Started	16
Completed	0
Not completed	16
Entered follow-up phase	-
Consent withdrawn by subject	-
Physician decision	-
Disease progression	13
Symptomatic deterioration	-
Death	1
Adverse event	1
Unspecified	1

Baseline characteristics

Reporting groups

Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	71	71	
Age categorical Units: Subjects			
Greater than or equal to(>=)1 to less than16 years	54	54	
>=16 to less than (<) 18 years	5	5	
>=18 to less than or equal (<=) to 21 years	12	12	
Gender categorical Units: Subjects			
Female	25	25	
Male	46	46	

Subject analysis sets

Subject analysis set title	Part 1
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects received temsirolimus intravenously once weekly over 60 minutes infusion in dose escalation schemes of 10 mg/m^2, 25 mg/m^2, 75 mg/m^2 and 150 mg/m^2.

Subject analysis set title	Part 2
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects with high-grade glioma, neuroblastoma and rhabdomyosarcoma were administered temsirolimus 75 mg/m^2 intravenously once weekly over 60 minutes infusion.

Reporting group values	Part 1	Part 2	
Number of subjects	19	52	
Age categorical Units: Subjects			
Greater than or equal to(>=)1 to less than16 years	12	42	
>=16 to less than (<) 18 years	2	3	
>=18 to less than or equal (<=) to 21 years	5	7	
Gender categorical Units: Subjects			
Female	8	17	
Male	11	35	

End points

End points reporting groups

Reporting group title	Temsirolimus 10 mg/m^2: Part 1
Reporting group description:	
Temsirolimus was administered intravenously over 60 minutes infusion.	
Reporting group title	Temsirolimus 25 mg/m^2: Part 1
Reporting group description:	
Temsirolimus was administered intravenously over 60 minutes infusion.	
Reporting group title	Temsirolimus 75 mg/m^2: Part 1
Reporting group description:	
Temsirolimus was administered intravenously over 60 minutes infusion.	
Reporting group title	Temsirolimus 150 mg/m^2: Part 1
Reporting group description:	
Temsirolimus was administered intravenously over 60 minutes infusion.	
Reporting group title	High-grade Glioma: Part 2
Reporting group description:	
Temsirolimus was administered intravenously to subjects with high-grade glioma over 60 minutes infusion.	
Reporting group title	Neuroblastoma: Part 2
Reporting group description:	
Temsirolimus was administered intravenously to subjects with neuroblatoma over 60 minutes infusion.	
Reporting group title	Rhabdomyosarcoma: Part 2
Reporting group description:	
Temsirolimus was administered intravenously to subjects with rhabdomyosarcoma over 60 minutes infusion.	
Subject analysis set title	Part 1
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects received temsirolimus intravenously once weekly over 60 minutes infusion in dose escalation schemes of 10 mg/m^2, 25 mg/m^2, 75 mg/m^2 and 150 mg/m^2.	
Subject analysis set title	Part 2
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects with high-grade glioma, neuroblastoma and rhabdomyosarcoma were administered temsirolimus 75 mg/m^2 intravenously once weekly over 60 minutes infusion.	

Primary: Number of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs): Part 1

End point title	Number of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs): Part 1[1][2]
End point description:	
An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. An SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged in patient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Safety population included all subjects who received at least 1 dose of study medication.	
End point type	Primary
End point timeframe:	
Baseline up to End of Treatment (EOT) (within 30 days of last dose)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be reported for this outcome.

[2] - 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: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	Temsirolimus 10 mg/m^2: Part 1	Temsirolimus 25 mg/m^2: Part 1	Temsirolimus 75 mg/m^2: Part 1	Temsirolimus 150 mg/m^2: Part 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	5	3	7
Units: subjects				
AEs	4	5	3	7
SAEs	2	2	2	3

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Drug Related Treatment Emergent Adverse Events (TEAEs): Part 1

End point title	Number of Subjects With Drug Related Treatment Emergent Adverse Events (TEAEs): Part 1[3][4]

End point description:

TEAEs are events that occurred on or after initial treatment that were absent before treatment or worsened during the treatment period relative to the pretreatment state. AEs that occurred within 30 days of the last administration of study treatment can be attributed to the treatment period. Safety population included all subjects who received at least 1 dose of study medication.

End point type	Primary

End point timeframe:

Baseline up to EOT (within 30 days of last dose)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be reported for this outcome.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	Temsirolimus 10 mg/m^2: Part 1	Temsirolimus 25 mg/m^2: Part 1	Temsirolimus 75 mg/m^2: Part 1	Temsirolimus 150 mg/m^2: Part 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	5	3	7
Units: subjects	4	5	3	7

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Drug Related Grade 3 and Higher Treatment Emergent Adverse Events (TEAEs): Part 1

End point title	Number of Subjects With Drug Related Grade 3 and Higher Treatment Emergent Adverse Events (TEAEs): Part 1[5][6]

End point description:

TEAEs are events that occurred on or after initial treatment that were absent before treatment or worsened during the treatment period relative to the pretreatment state. AEs that occurred within 30 days of the last administration of study treatment can be attributed to the treatment period. National Cancer Institute (NCI)-graded Common Toxicity Criteria (CTC) provides descriptive terminology for adverse event
reporting. A grading (severity) scale is provided for each adverse event term. Grades range from 0 (none) to 5 (death). Safety population included all subjects who received at least 1 dose of study medication.

End point type	Primary

End point timeframe:

Baseline up to EOT (within 30 days of last dose)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be reported for this outcome.

[6] - 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: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	Temsirolimus 10 mg/m^2: Part 1	Temsirolimus 25 mg/m^2: Part 1	Temsirolimus 75 mg/m^2: Part 1	Temsirolimus 150 mg/m^2: Part 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	5	3	7
Units: subjects	1	2	2	4

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Who Died: Part 1

End point title	Number of Subjects Who Died: Part 1[7][8]

End point description:

Deaths were reported from baseline throughout the 30 day period after last study treatment. After the 30 day reporting period, only deaths believed related to study treatment were to be reported (as SAEs). Safety population included all subjects who received at least 1 dose of study medication.

End point type	Primary

End point timeframe:

Baseline up to EOT (within 30 days of last dose)

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

[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: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	Temsirolimus 10 mg/m^2: Part 1	Temsirolimus 25 mg/m^2: Part 1	Temsirolimus 75 mg/m^2: Part 1	Temsirolimus 150 mg/m^2: Part 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	5	3	7
Units: subjects				
Died=Yes	3	1	0	0
Died within 30 days of last dose	2	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Drug Related Serious Adverse Events (SAEs): Part 1

End point title	Number of Subjects With Drug Related Serious Adverse Events (SAEs): Part 1[9][10]

End point description:

SAEs include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability / incapacity or are a congenital anomaly or birth defect in the offspring of a study subject. Subjects with documented study treatment toxicity were followed weekly until recovering. After the 30 day reporting period, only SAEs believed to be related to study treatment were to be reported. Safety population included all subjects who received at least 1 dose of study medication.

End point type	Primary

End point timeframe:

Baseline up to EOT (within 30 days of last dose)

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be reported for this outcome.

[10] - 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: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	Temsirolimus 10 mg/m^2: Part 1	Temsirolimus 25 mg/m^2: Part 1	Temsirolimus 75 mg/m^2: Part 1	Temsirolimus 150 mg/m^2: Part 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	5	3	7
Units: subjects	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Adverse Events Causing Temporary Stop of Study Treatment: Part 1

End point title	Number of Subjects With Adverse Events Causing Temporary Stop of Study Treatment: Part 1[11][12]

End point description:

Temporary interruption of study treatment; may be followed by resumption of study treatment at current dose or dose modification as determined by the investigator and medical monitor. Safety population included all subjects who received at least 1 dose of study medication.

End point type	Primary

End point timeframe:

Baseline up to EOT (within 30 days of last dose)

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be reported for this outcome.

[12] - 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: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	Temsirolimus 10 mg/m^2: Part 1	Temsirolimus 25 mg/m^2: Part 1	Temsirolimus 75 mg/m^2: Part 1	Temsirolimus 150 mg/m^2: Part 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	5	3	7
Units: subjects	0	2	1	2

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Adverse Events Causing Dose Reduction of Study Treatment: Part 1

End point title	Number of Subjects With Adverse Events Causing Dose Reduction of Study Treatment: Part 1[13][14]

End point description:

Dose reduction for individual subject allowed if a dose limiting toxicity (DLT) occurred; may continue treatment following reduction by 1 to 2 dose levels (determined by investigator and medical monitor). DLT= failure to recover to National Cancer Institute Common Terminology Criteria for AEs (NCI-CTCAE) version 3.0 grade 0 to 2 (or within 1 grade of starting values for pre-existing laboratory abnormalities) from a treatment-related toxicity within 3 weeks (leading to a treatment delay of >3 weeks) unless investigator and medical monitor agree subject should remain in the study. Safety population included all subjects who received at least 1 dose of study medication.

End point type	Primary

End point timeframe:

Baseline up to EOT (within 30 days of last dose)

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be reported for this outcome.

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	Temsirolimus 10 mg/m^2: Part 1	Temsirolimus 25 mg/m^2: Part 1	Temsirolimus 75 mg/m^2: Part 1	Temsirolimus 150 mg/m^2: Part 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	5	3	7
Units: subjects	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Potentially Clinically Important (PCI) Changes in Vital Signs: Part 1

End point title	Number of Subjects With Potentially Clinically Important (PCI) Changes in Vital Signs: Part 1[15][16]

End point description:

Number of subjects who met the criteria for PCI changes (based on baseline values before treatment); criteria defined as body temperature greater than (>) 39 degrees Celsius (C), respiratory rate >20 beats per minute (bpm), and systolic and diastolic blood pressure (BP) >200/110 millimeters of mercury (mmHg). Subjects may be reported in more than 1 category. Safety population included all subjects who received at least 1 dose of study medication.

End point type	Primary

End point timeframe:

Baseline up to EOT (within 30 days of last dose)

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be reported for this outcome.

[16] - 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: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	Temsirolimus 10 mg/m^2: Part 1	Temsirolimus 25 mg/m^2: Part 1	Temsirolimus 75 mg/m^2: Part 1	Temsirolimus 150 mg/m^2: Part 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	5	3	7
Units: subjects				
Temperature >39 degrees C	1	2	1	3
Respiratory rate >20 bpm	4	5	3	7
Systolic/Diastolic BP >200/110 mmHg	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Potentially Clinically Important (PCI) Values by National Cancer Institute Common Terminology Criteria (NCI-CTC) Grade for Laboratory Values: Part 1

End point title	Number of Subjects With Potentially Clinically Important (PCI)

	Values by National Cancer Institute Common Terminology Criteria (NCI-CTC) Grade for Laboratory Values: Part 1[17][18]

End point description:

Number of subjects who met the PCI criteria (grades 1 through 5) for laboratory values (hematology and serum chemistry). NCI-CTC provides descriptive terminology for adverse event reporting. A grading (severity) scale is provided with grades ranging from 0 (none), 1 (mild), 2 (moderate), 3 (severe), 4 (life-threatening or disabling), to 5 (death). Subjects may be reported in more than 1 category. Safety population included all subjects who received at least 1 dose of study medication.

End point type	Primary

End point timeframe:

Baseline up to EOT (within 30 days of last dose)

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be reported for this outcome.

[18] - 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: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	Temsirolimus 10 mg/m^2: Part 1	Temsirolimus 25 mg/m^2: Part 1	Temsirolimus 75 mg/m^2: Part 1	Temsirolimus 150 mg/m^2: Part 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	5	3	7
Units: subjects	4	5	3	7

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Objective Response (OR) at Week 12: Part 2

End point title	Percentage of Subjects With Objective Response (OR) at Week 12: Part 2[19][20]

End point description:

Measured as Complete response (CR), Very good partial response (VGPR), or PR on at least 2 occasions >= 4 weeks apart within first 12 weeks. CR=disappearance of all primary and metastatic lesions; Homovanillic acid, Vanillymandelic acid (HVA/VMA) normal; bone marrow immunocytology negative. VGPR=disappearance of all metastatic lesions (residual areas of uptake on bone permitted); 90 to 99 percent (%) decrease in primary disease measurement; HVA/VMA normal or both decreased >90%. PR=at least 50% decrease in primary and metastatic disease. Number of bone sites decreased by at least 50%. Efficacy evaluable population included all subjects who received at least 3 doses of study treatment.

End point type	Primary

End point timeframe:

Week 12

Notes:

[19] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be reported for this outcome.

[20] - 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: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	High-grade Glioma: Part 2	Neuroblastoma: Part 2	Rhabdomyosarcoma: Part 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15[21]	15[22]	12[23]	
Units: percentage of subjects				
number (not applicable)	0	6.67	0	

Notes:

[21] - N= Number of subjects who were evaluable for this measure for each group respectively.

[22] - N= Number of subjects who were evaluable for this measure for each group respectively..

[23] - N= Number of subjects who were evaluable for this measure for each group respectively.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Reached Maximum Tolerated Dose Due to Dose Limiting Toxicity: Part 1

End point title	Number of Subjects Who Reached Maximum Tolerated Dose Due to Dose Limiting Toxicity: Part 1[24]

End point description:

Maximum tolerated dose (MTD) defined as the dose level at which >=2 of 3 subjects or >=2 of 6 subjects if the dose level had been expanded, experienced a dose limiting toxicity (DLT) by day 21 after the first dose of study treatment. DLT defined as failure to recover to NCI-CTCAE version 3.0 grade 0 to 2 (or within 1 grade of starting values for pre-existing laboratory abnormalities) from a treatment-related toxicity within 3 weeks (leading to a treatment delay of > 3 weeks) unless the investigator and the medical monitor agree that the subject should remain in the study. Safety population included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Baseline up to Month 6

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	Temsirolimus 10 mg/m^2: Part 1	Temsirolimus 25 mg/m^2: Part 1	Temsirolimus 75 mg/m^2: Part 1	Temsirolimus 150 mg/m^2: Part 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	5	3	7
Units: subjects	0	0	0	2

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Whole Blood Concentration (Cmax): Part 1

End point title	Maximum Observed Whole Blood Concentration (Cmax): Part

End point description:

Safety population included all subjects who received at least 1 dose of study medication. Here, 'n' signifies those subjects who were evaluable for particular cycle for each group respectively.

End point type	Secondary

End point timeframe:

0 (pre-dose), 1, 2, 6, 24, and 168 hours (hrs) post-dose of Cycle 1 and 0 (pre-dose), 1, 2, 6, 24, 72, 96, and 168 hrs post-dose of Cycle 2 (cycles are approximately 21 days)

Notes:

[25] - 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: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	Temsirolimus 10 mg/m^2: Part 1	Temsirolimus 25 mg/m^2: Part 1	Temsirolimus 75 mg/m^2: Part 1	Temsirolimus 150 mg/m^2: Part 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	5	3	7
Units: nanogram per millilitre (ng/mL)				
arithmetic mean (standard deviation)				
Cycle 1 (n = 4, 5, 3, 7)	307 (± 91.3)	487 (± 141)	480 (± 135)	9230 (± 18200)
Cycle 2 (n = 4, 4, 3, 5)	252 (± 98.3)	403 (± 128)	807 (± 279)	2570 (± 1110)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Observed Whole Blood Concentration (Tmax): Part 1

End point title	Time to Reach Maximum Observed Whole Blood Concentration (Tmax): Part 1[26]

End point description:

Safety population included all subjects who received at least 1 dose of study medication. Here, 'n' signifies those subjects who were evaluable for particular cycle for each group respectively.

End point type	Secondary

End point timeframe:

0 (pre-dose), 1, 2, 6, 24, and 168 hrs post-dose of Cycle 1 and 0 (pre-dose), 1, 2, 6, 24, 72, 96, and 168 hrs post-dose of Cycle 2 (cycles are approximately 21 days)

Notes:

[26] - 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: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	Temsirolimus 10 mg/m^2: Part 1	Temsirolimus 25 mg/m^2: Part 1	Temsirolimus 75 mg/m^2: Part 1	Temsirolimus 150 mg/m^2: Part 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	5	3	7
Units: hr				
arithmetic mean (standard deviation)				
Cycle 1 (n = 4, 5, 3, 7)	1 (± 0.143)	1.1 (± 0.074)	1.3 (± 0.231)	1.1 (± 0.218)
Cycle 2 (n = 4, 4, 3, 5)	1.1 (± 0.236)	1.7 (± 0.983)	1.2 (± 0.202)	1.2 (± 0.212)

Statistical analyses

No statistical analyses for this end point

Secondary: Half-Life (t1/2): Part 1

End point title	Half-Life (t1/2): Part 1[27]

End point description:

Plasma decay half-life is the time measured for the whole blood concentration to decrease by one half. Safety population included all subjects who received at least 1 dose of study medication. Here, 'n' signifies those subjects who were evaluable for particular cycle for each group respectively. Here 99999 in standard deviation (SD) signifies that data was not estimable. SD was not estimable since only 1 subject was evaluable.

End point type	Secondary

End point timeframe:

0 (pre-dose), 1, 2, 6, 24, and 168 hrs post-dose of Cycle 1 and 0 (pre-dose), 1, 2, 6, 24, 72, 96, and 168 hrs post-dose of Cycle 2 (cycles are approximately 21 days)

Notes:

[27] - 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: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	Temsirolimus 10 mg/m^2: Part 1	Temsirolimus 25 mg/m^2: Part 1	Temsirolimus 75 mg/m^2: Part 1	Temsirolimus 150 mg/m^2: Part 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[28]	4[29]	3[30]	5[31]
Units: hr				
arithmetic mean (standard deviation)				
Cycle 1 (n = 4, 4, 1, 4)	10.6 (± 0.556)	16.4 (± 6.9)	24 (± 99999)	19.3 (± 10.5)
Cycle 2 (n = 4, 3, 3, 5)	14.4 (± 4.42)	14.3 (± 10.4)	25.4 (± 1.83)	24.2 (± 7.58)

Notes:

[28] - N= Number of subjects who were evaluable for this measure for each group respectively.

[29] - N= Number of subjects who were evaluable for this measure for each group respectively.

[30] - N= Number of subjects who were evaluable for this measure for each group respectively.

[31] - N= Number of subjects who were evaluable for this measure for each group respectively..

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Curve From Time Zero to Last Quantifiable Concentration [AUC (0-t)]: Part 1

End point title	Area Under the Curve From Time Zero to Last Quantifiable Concentration [AUC (0-t)]: Part 1[32]

End point description:

AUC (0-t)= Area under the whole blood concentration versus time curve from time zero (pre-dose) to time of last quantifiable concentration (0-t). Safety population included all subjects who received at least 1 dose of study medication. Here, 'n' signifies those subjects who were evaluable for particular cycle for each group respectively.

End point type	Secondary

End point timeframe:

0 (pre-dose), 1, 2, 6, 24, and 168 hrs post-dose of Cycle 1 and 0 (pre-dose), 1, 2, 6, 24, 72, 96, and 168 hrs post-dose of Cycle 2 (cycles are approximately 21 days)

Notes:

[32] - 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: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	Temsirolimus 10 mg/m^2: Part 1	Temsirolimus 25 mg/m^2: Part 1	Temsirolimus 75 mg/m^2: Part 1	Temsirolimus 150 mg/m^2: Part 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	5	3	7
Units: hr*ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 (n = 4, 5, 3, 7)	1670 (± 730)	3890 (± 3190)	3750 (± 2420)	9680 (± 12800)
Cycle 2 (n = 4, 4, 3, 5)	1520 (± 583)	1930 (± 1090)	3420 (± 1230)	4850 (± 1810)

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration-Time Curve (AUC): Part 1

End point title	Area Under the Concentration-Time Curve (AUC): Part 1[33]

End point description:

AUC= Area under the concentration versus time curve from time zero (pre-dose) over time. It is used to characterize extent of exposure. Safety population included all subjects who received at least 1 dose of study medication. Here, 'n' signifies those subjects who were evaluable for particular cycle for each group respectively. 99999 in standard deviation (SD) signifies that data was not estimable. SD was not estimable since only 1 subject was evaluable.

End point type	Secondary

End point timeframe:

0 (pre-dose), 1, 2, 6, 24, and 168 hrs post-dose of Cycle 1 and 0 (pre-dose), 1, 2, 6, 24, 72, 96, and 168 hrs post-dose of Cycle 2 (cycles are approximately 21 days)

Notes:

[33] - 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: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	Temsirolimus 10 mg/m^2: Part 1	Temsirolimus 25 mg/m^2: Part 1	Temsirolimus 75 mg/m^2: Part 1	Temsirolimus 150 mg/m^2: Part 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[34]	4[35]	3[36]	5[37]
Units: hr*ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 (n = 4, 4, 1, 4)	2000 (± 959)	4640 (± 3430)	2810 (± 99999)	13000 (± 17000)
Cycle 2 (n = 4, 3, 3, 5)	1600 (± 540)	2580 (± 768)	3500 (± 1140)	4960 (± 2000)

Notes:

[34] - N= Number of subjects who were evaluable for this measure for each group respectively.

[35] - N= Number of subjects who were evaluable for this measure for each group respectively.

[36] - N= Number of subjects who were evaluable for this measure for each group respectively.

[37] - N= Number of subjects who were evaluable for this measure for each group respectively.

Statistical analyses

No statistical analyses for this end point

Secondary: Clearance (CL): Part 1

End point title	Clearance (CL): Part 1[38]

End point description:

CL is a hypothetical volume of blood that is cleared of drug in a given unit of time. Safety population included all subjects who received at least 1 dose of study medication. Here, 'n' signifies those subjects who were evaluable for particular cycle for each group respectively. Here 99999 in standard deviation (SD) signifies that data was not estimable. SD was not estimable since only 1 subject was evaluable.

End point type	Secondary

End point timeframe:

0 (pre-dose), 1, 2, 6, 24, and 168 hrs post-dose of Cycle 1 and 0 (pre-dose), 1, 2, 6, 24, 72, 96, and 168 hrs post-dose of Cycle 2 (cycles are approximately 21 days)

Notes:

[38] - 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: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	Temsirolimus 10 mg/m^2: Part 1	Temsirolimus 25 mg/m^2: Part 1	Temsirolimus 75 mg/m^2: Part 1	Temsirolimus 150 mg/m^2: Part 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[39]	4[40]	3[41]	5[42]
Units: liter/hr (L/hr)				
arithmetic mean (standard deviation)				
Cycle 1 (n = 4, 4, 1, 4)	7.02 (± 3.68)	10.4 (± 6.45)	38.1 (± 99999)	47.9 (± 45.8)
Cycle 2 (n = 4, 3, 3, 5)	8.99 (± 5.27)	13.8 (± 9.06)	30.6 (± 15.5)	39 (± 24.4)

Notes:

[39] - N= Number of subjects who were evaluable for this measure for each group respectively.

[40] - N= Number of subjects who were evaluable for this measure for each group respectively.

[41] - N= Number of subjects who were evaluable for this measure for each group respectively.

[42] - N= Number of subjects who were evaluable for this measure for each group respectively.

Statistical analyses

No statistical analyses for this end point

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

End point title	Volume of Distribution at Steady State (Vss): Part 1[43]

End point description:

Volume of distribution is defined as the theoretical volume in which the total amount of drug would need to be uniformly distributed to produce the desired blood concentration of a drug. Steady state volume of distribution (Vss) is the apparent volume of distribution at steady-state. Safety population included all subjects who received at least 1 dose of study medication. Here, 'n' signifies those subjects who were evaluable for particular cycle for each group respectively. 99999 in standard deviation (SD) signifies that data was not estimable. SD was not estimable since only 1 subject was evaluable.

End point type	Secondary

End point timeframe:

0 (pre-dose), 1, 2, 6, 24, and 168 hrs post-dose of Cycle 1 and 0 (pre-dose), 1, 2, 6, 24, 72, 96, and 168 hrs post-dose of Cycle 2 (cycles are approximately 21 days)

Notes:

[43] - 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: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	Temsirolimus 10 mg/m^2: Part 1	Temsirolimus 25 mg/m^2: Part 1	Temsirolimus 75 mg/m^2: Part 1	Temsirolimus 150 mg/m^2: Part 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[44]	4[45]	3[46]	5[47]
Units: liter				
arithmetic mean (standard deviation)				
Cycle 1 (n = 4, 4, 1, 4)	85.2 (± 35)	189 (± 44.2)	783 (± 99999)	512 (± 689)
Cycle 2 (n = 4, 3, 3, 5)	250 (± 290)	201 (± 132)	601 (± 347)	353 (± 130)

Notes:

[44] - N= Number of subjects who were evaluable for this measure for each group respectively.

[45] - N= Number of subjects who were evaluable for this measure for each group respectively.

[46] - N= Number of subjects who were evaluable for this measure for each group respectively.

[47] - N= Number of subjects who were evaluable for this measure for each group respectively.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Best Overall Response: Part 1

End point title	Percentage of Subjects With Best Overall Response: Part 1[48]

End point description:

Best overall response is the best response recorded from baseline until disease progression or recurrence. Measured as CR, PR, Stable Disease (SD), Progressive Disease (PD), or Unknown. CR=disappearance of all primary and metastatic lesions. PR=at least a 50% decrease in primary disease measurement. SD=no new lesions; decrease of <50% in all lesions with no lesion increasing >25%. PD=any new lesion; at least a 25% increase in any disease measurement (reference smallest disease measurement recorded since start of treatment); or appearance of 1 or more new lesions. Tumor response considered Unknown if assessment prior to Day 37. Safety population included all subjects who received at least 1 dose of study medication. Here, 'n' signifies those subjects who were evaluable for particular cycle for each group respectively.

End point type	Secondary

End point timeframe:

Baseline until disease progression or recurrence (actual greatest response day is up to Day 49)

Notes:

[48] - 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: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	Temsirolimus 10 mg/m^2: Part 1	Temsirolimus 25 mg/m^2: Part 1	Temsirolimus 75 mg/m^2: Part 1	Temsirolimus 150 mg/m^2: Part 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[49]	4[50]	3[51]	7[52]
Units: percentage of subjects				
number (not applicable)				

Complete response	1	0	0	0
Partial response	0	0	0	0
Stable disease	0	2	3	2
Progressive disease	3	2	0	3
Unknown response	0	0	0	2

Notes:

[49] - N= Number of subjects who were evaluable for this measure for each group respectively.

[50] - N= Number of subjects who were evaluable for this measure for each group respectively.

[51] - N= Number of subjects who were evaluable for this measure for each group respectively.

[52] - N= Number of subjects who were evaluable for this measure for each group respectively.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Exhibiting Freedom From Progression at Week 12: Part 2

End point title	Percentage of Subjects Exhibiting Freedom From Progression at Week 12: Part 2[53]

End point description:

Freedom from progression measured as Stable Disease (SD) or better and no Progressive Disease (PD); (CR+VGPR+Mixed Response [MR]+PR+SD). CR=disappearance of all primary and metastatic lesions. VGPR=disappearance of all metastatic lesions. MR=no new lesions; at least 50% decrease in any 1 disease measurement with <50% decrease in any other disease measurement or an increase of <25% in any lesion). SD=no new lesions; decrease of <50% in all lesions with no lesion increasing >25%. PD=at least a 25% increase in any disease measurement; or the appearance of 1 or more new lesions. Efficacy evaluable population included all subjects who received at least 3 doses of study treatment.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[53] - 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: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	High-grade Glioma: Part 2	Neuroblastoma: Part 2	Rhabdomyosarcoma: Part 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15[54]	15[55]	15[56]	
Units: percentage of subjects				
number (confidence interval 95%)	46.67 (21.27 to 73.41)	40 (16.34 to 67.71)	8.33 (0.21 to 38.48)	

Notes:

[54] - N= Number of subjects who were evaluable for this measure for each group respectively.

[55] - N= Number of subjects who were evaluable for this measure for each group respectively.

[56] - N= Number of subjects who were evaluable for this measure for each group respectively.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs): Part 2

End point title	Number of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs): Part 2[57]

End point description:

An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. An SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Safety population included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Baseline up to EOT (within 30 days of last dose)

Notes:

[57] - 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: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	High-grade Glioma: Part 2	Neuroblastoma: Part 2	Rhabdomyosarcoma: Part 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	19	16	
Units: subjects				
AEs	17	19	16	
SAEs	10	6	6	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Drug Related Treatment Emergent Adverse Events (TEAEs): Part 2

End point title	Number of Subjects With Drug Related Treatment Emergent Adverse Events (TEAEs): Part 2[58]

End point description:

Treatment-emergent are events between first dose of study drug and up to 30 days after last dose that were absent before treatment or that worsened relative to pretreatment state. Safety population included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Baseline up to EOT (within 30 days of last dose)

Notes:

[58] - 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: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	High-grade Glioma: Part 2	Neuroblastoma: Part 2	Rhabdomyosarcoma: Part 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	19	16	
Units: subjects	17	18	13	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Drug Related Grade 3 and Higher Treatment Emergent Adverse Events (TEAEs): Part 2

End point title	Number of Subjects With Drug Related Grade 3 and Higher Treatment Emergent Adverse Events (TEAEs): Part 2[59]

End point description:

Treatment-emergent are events between first dose of study drug and up to 30 days after last dose that were absent before treatment or that worsened relative to pretreatment state. NCI-CTC provides descriptive terminology for adverse event reporting. A grading (severity) scale was provided for each adverse event term. Grades range from 0 (none) to 5 (death). Safety population included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Baseline up to EOT (within 30 days of last dose)

Notes:

[59] - 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: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	High-grade Glioma: Part 2	Neuroblastoma: Part 2	Rhabdomyosarcoma: Part 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	19	16	
Units: subjects	5	11	6	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Died: Part 2

End point title	Number of Subjects Who Died: Part 2[60]

End point description:

Deaths were reported from baseline throughout the 30 day period after last study treatment. After the 30 day reporting period, only deaths believed related to study treatment were to be reported (as SAEs). Safety population included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Baseline up to EOT (within 30 days of last dose)

Notes:

[60] - 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: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	High-grade Glioma: Part 2	Neuroblastoma: Part 2	Rhabdomyosarcoma: Part 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	19	16	
Units: subjects				
Died=Yes	5	2	4	
Died within 30 days of last dose	3	0	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Drug Related Serious Adverse Events (SAEs): Part 2

End point title	Number of Subjects With Drug Related Serious Adverse Events (SAEs): Part 2[61]

End point description:

An SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Subjects with documented study treatment toxicity were followed weekly until recovering. After the 30 day reporting period, only SAEs believed to be related to study treatment were to be reported. Safety population included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Baseline up to EOT (within 30 days of last dose)

Notes:

[61] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	High-grade Glioma: Part 2	Neuroblastoma: Part 2	Rhabdomyosarcoma: Part 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	19	16	
Units: subjects	2	3	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Adverse Events Causing Temporary Stop of Study Treatment: Part 2

End point title	Number of Subjects With Adverse Events Causing Temporary Stop of Study Treatment: Part 2[62]

End point description:

An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. Temporary interruption of study treatment may be followed by resumption of study treatment at current dose or dose modification as determined by the investigator and medical monitor. Safety population included all subjects who received at least 1 dose of study

medication.

End point type	Secondary

End point timeframe:

Baseline up to EOT (within 30 days of last dose)

Notes:

[62] - 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: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	High-grade Glioma: Part 2	Neuroblastoma: Part 2	Rhabdomyosarcoma: Part 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	19	16	
Units: subjects	9	12	6	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Adverse Events Causing Dose Reduction of Study Treatment: Part 2

End point title	Number of Subjects With Adverse Events Causing Dose Reduction of Study Treatment: Part 2[63]

End point description:

Dose reduction for individual subject allowed if a DLT occurred; may continue treatment following reduction by 1 to 2 dose levels (determined by investigator and medical monitor). DLT= failure to recover to National Cancer Institute Common Terminology Criteria for AEs (NCI-CTCAE) version 3.0 grade 0 to 2 (or within 1 grade of starting values for pre-existing laboratory abnormalities) from a treatment-related toxicity within 3 weeks (leading to a treatment delay of >3 weeks) unless investigator and medical monitor agree subject should remain in the study. Safety population included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Baseline up to EOT (within 30 days of last dose)

Notes:

[63] - 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: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	High-grade Glioma: Part 2	Neuroblastoma: Part 2	Rhabdomyosarcoma: Part 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	19	16	
Units: subjects	5	10	6	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Potentially Clinically Important (PCI) Changes in Vital Signs: Part 2

End point title	Number of Subjects With Potentially Clinically Important (PCI) Changes in Vital Signs: Part 2[64]

End point description:

Number of subjects who met the criteria for PCI changes (based on baseline values before treatment); criteria defined as body temperature >39 degrees C, respiratory rate >20 bpm, and systolic and diastolic BP >200/110 mmHg. Subjects may be reported in more than 1 category. Safety population included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Baseline up to EOT (within 30 days of last dose)

Notes:

[64] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	High-grade Glioma: Part 2	Neuroblastoma: Part 2	Rhabdomyosarcoma: Part 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	19	16	
Units: subjects				
Temperature >39 degrees C	0	0	0	
Respiratory rate >20 bpm	16	18	14	
Systolic/Diastolic BP >200/110 mmHg	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Potentially Clinically Important (PCI) Values by National Cancer Institute Common Terminology Criteria (NCI-CTC) Grade for Laboratory Values: Part 2

End point title	Number of Subjects With Potentially Clinically Important (PCI) Values by National Cancer Institute Common Terminology Criteria (NCI-CTC) Grade for Laboratory Values: Part 2[65]

End point description:

Number of subjects who met the PCI criteria (grades 1 through 5) for laboratory values (hematology and serum chemistry). NCI-CTC provides descriptive terminology for adverse event reporting. A grading (severity) scale is provided with grades ranging from 0 (none), 1 (mild), 2 (moderate), 3 (severe), 4 (life-threatening or disabling), to 5 (death). Subjects were reported in more than 1 category. Safety population included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Baseline up to EOT (within 30 days of last dose)

Notes:

[65] - 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: This endpoint was planned to be analyzed in Part 1 and Part 2 separately.

End point values	High-grade Glioma: Part 2	Neuroblastoma: Part 2	Rhabdomyosarcoma: Part 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	19	16	
Units: subjects	17	19	15	

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Whole Blood Concentration (Cmax): Part 2

End point title	Maximum Observed Whole Blood Concentration (Cmax): Part 2

End point description:

Safety population included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

0 (pre-dose), 1, 6, 24, 48, 72, 96, and 168 hrs post-dose of Cycle 2 (cycles are approximately 21 days)

End point values	Part 2			
Subject group type	Subject analysis set			
Number of subjects analysed	35[66]			
Units: ng/mL				
arithmetic mean (standard deviation)	6280 (± 21000)			

Notes:

[66] - N= Number of subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Average Whole Blood Concentration (Cavg): Part 2

End point title	Average Whole Blood Concentration (Cavg): Part 2

End point description:

Safety population included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

0 (pre-dose), 1, 6, 24, 48, 72, 96, and 168 hrs post-dose of Cycle 2 (cycles are approximately 21 days)

End point values	Part 2			
Subject group type	Subject analysis set			
Number of subjects analysed	31[67]			
Units: ng/mL				
arithmetic mean (standard deviation)	82.8 (± 143)			

Notes:

[67] - N= Number of subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Observed Whole Blood Concentration (Tmax): Part 2

End point title	Time to Reach Maximum Observed Whole Blood Concentration (Tmax): Part 2

End point description:

Safety population included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

0 (pre-dose),1, 6, 24, 48, 72, 96, and 168 hrs post-dose of Cycle 2 (cycles are approximately 21 days)

End point values	Part 2			
Subject group type	Subject analysis set			
Number of subjects analysed	35[68]			
Units: hours				
median (full range (min-max))	1 (0 to 6)			

Notes:

[68] - N= Number of subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Half-Life (t1/2): Part 2

End point title	Half-Life (t1/2): Part 2

End point description:

Half-life is the time measured for the whole blood concentration to decrease by one half. Safety population included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

0 (pre-dose), 1, 6, 24, 48, 72, 96, and 168 hrs post-dose of Cycle 2 (cycles are approximately 21 days)

End point values	Part 2			
Subject group type	Subject analysis set			
Number of subjects analysed	26[69]			
Units: hours				
arithmetic mean (standard deviation)	30.65 (± 13.63)			

Notes:

[69] - N= Number of subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Curve From Time Zero to Last Quantifiable Concentration [AUC (0-t)]: Part 2

End point title	Area Under the Curve From Time Zero to Last Quantifiable Concentration [AUC (0-t)]: Part 2

End point description:

AUC (0-t)= Area under the whole blood concentration versus time curve from time zero (pre-dose) to time of last quantifiable concentration (0-t). Safety population included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

0 (pre-dose), 1, 6, 24, 48, 72, 96, and 168 hrs post-dose of Cycle 2 (cycles are approximately 21 days)

End point values	Part 2			
Subject group type	Subject analysis set			
Number of subjects analysed	35[70]			
Units: hr*ng/mL				
arithmetic mean (standard deviation)	13100 (± 22700)			

Notes:

[70] - N= Number of subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration-time Curve at Steady State (AUCss): Part 2

End point title	Area Under the Concentration-time Curve at Steady State (AUCss): Part 2

End point description:

AUCss is the area under the drug concentration in whole blood versus time curve over one dosage interval at steady-state. It is used to characterize extent of exposure. Safety population included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

0 (pre-dose), 1, 6, 24, 48, 72, 96, and 168 hrs post-dose of Cycle 2 (cycles are approximately 21 days)

End point values	Part 2			
Subject group type	Subject analysis set			
Number of subjects analysed	31[71]			
Units: hr*ng/mL				
arithmetic mean (standard deviation)	13900 (± 24100)			

Notes:

[71] - N= Number of subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Clearance (CL): Part 2

End point title	Clearance (CL): Part 2

End point description:

CL is a hypothetical volume of blood that is cleared of drug in a given unit of time. Safety population included all subjects who received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

0 (pre-dose),1, 6, 24, 48, 72, 96, and 168 hrs post-dose of Cycle 2 (cycles are approximately 21 days)

End point values	Part 2			
Subject group type	Subject analysis set			
Number of subjects analysed	31[72]			
Units: L/hr				
arithmetic mean (standard deviation)	14.3 (± 14)			

Notes:

[72] - N= Number of subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration in Whole Blood (Cp) and Concentration in Whole Blood at Time Zero (Cp Time 0): Part 1 and Part 2

End point title	Concentration in Whole Blood (Cp) and Concentration in Whole Blood at Time Zero (Cp Time 0): Part 1 and Part 2

End point description:

Pharmacokinetic parameters determined in whole blood; derived from the concentration-versus-time profiles using noncompartmental analysis method. Measured as ng/mL.

End point type	Secondary

End point timeframe:

Part 1: 0 (pre-dose), 1, 2, 6, 24, and 168 hrs post-dose of Cycle 1 and 0 (pre-dose), 1, 2, 6, 24, 72, 96, and 168 hrs post-dose of Cycle 2; Part2: 0 (pre-dose), 1, 6, 24, 48, 72, 96, and 168 hrs post-dose of

End point values	Part 1	Part 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[73]	0[74]		
Units: subjects				

Notes:

[73] - Data was not analyzed for this outcome measure.

[74] - Data was not analyzed for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects for Change From Baseline in the Phosphorylation of Mammalian Target of Rapamycin (mTOR) Pathway Proteins: Part 1 and Part 2

End point title	Number of Subjects for Change From Baseline in the Phosphorylation of Mammalian Target of Rapamycin (mTOR) Pathway Proteins: Part 1 and Part 2

End point description:

Optional bone marrow sampling for pharmacodynamic analysis of effects of study treatment. Data may not be collected for a majority of subjects and was not to be summarized if collection was sparse.

End point type	Secondary

End point timeframe:

Part 1:Baseline,1,2,6,24,168 hrs post-dose of Cycle 1;additional 0 (Pre-dose),24,72,96 hrs, Day 16 to 21 of cycle 2, EOT(within 30 days of last dose); Part 2:Baseline,Day16 to 21 in Cycle 2, at time of disease progression, EOT(within 30 days of last dose)

End point values	Part 1	Part 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[75]	0[76]		
Units: subjects				

Notes:

[75] - Data was not analyzed for this outcome measure.

[76] - Data was not analyzed for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 30 days after last dose of study drug

Adverse event reporting additional description:

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

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Temsirolimus 10mg/m2: Part 1

Reporting group description:

Temsirolimus 10 mg/m^2 administered intravenously once weekly over 60 minutes infusion.

Reporting group title	Temsirolimus 25mg/m2: Part 1

Reporting group description:

Temsirolimus 25 mg/m^2 administered intravenously once weekly over 60 minutes infusion.

Reporting group title	Temsirolimus 75mg/m2: Part 1

Reporting group description:

Temsirolimus 75 mg/m^2 administered intravenously once weekly over 60 minutes infusion.

Reporting group title	Temsirolimus 150mg/m2: Part 1

Reporting group description:

Temsirolimus 150 mg/m^2 intravenously administered once weekly over 60 minutes infusion.

Reporting group title	High-grade Glioma: Part 2

Reporting group description:

Subjects with high-grade glioma were administered temsirolimus 75 mg/m^2 intravenously once weekly over 60 minutes infusion.

Reporting group title	Neuroblastoma: Part 2

Reporting group description:

Subjects with neuroblastoma were administered temsirolimus 75 mg/m^2 intravenously once weekly over 60 minutes infusion.

Reporting group title	Rhabdomyosarcoma: Part 2

Reporting group description:

Subjects with rhabdomyosarcoma were administered temsirolimus 75 mg/m^2 intravenously once weekly over 60 minutes infusion.

Serious adverse events	Temsirolimus 10mg/m2: Part 1	Temsirolimus 25mg/m2: Part 1	Temsirolimus 75mg/m2: Part 1
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 4 (50.00%)	2 / 5 (40.00%)	2 / 3 (66.67%)
number of deaths (all causes)	2	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Rhabdomyosarcoma			

subjects affected / exposed	1 / 4 (25.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour associated fever			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Pain management			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Fatigue			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemothorax			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Interstitial lung disease			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Electrocardiogram abnormal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Brain herniation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiopulmonary failure			

subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular dysfunction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Central nervous system haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coordination abnormal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drooling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			

subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Somnolence			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salivary hypersecretion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			

subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nail infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophosphataemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Temsirolimus 150mg/m2: Part 1	High-grade Glioma: Part 2	Neuroblastoma: Part 2
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 7 (42.86%)	10 / 17 (58.82%)	8 / 19 (42.11%)
number of deaths (all causes)	0	3	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Rhabdomyosarcoma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour associated fever			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	3 / 19 (15.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	0 / 7 (0.00%)	2 / 17 (11.76%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (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
Surgical and medical procedures			
Pain management			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	0 / 19 (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
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (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
Pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	0 / 19 (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
Peripheral swelling			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (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

Pyrexia			
subjects affected / exposed	1 / 7 (14.29%)	1 / 17 (5.88%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	2 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemothorax			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (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
Interstitial lung disease			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory distress			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Investigations			
Electrocardiogram abnormal			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Brain herniation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiopulmonary failure			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular dysfunction			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Central nervous system haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (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
Coordination abnormal			

subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (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
Drooling			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (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
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 7 (14.29%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	0 / 19 (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
Seizure			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Somnolence			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			

subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
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	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salivary hypersecretion			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Urinary retention			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (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
Endocrine disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	1 / 7 (14.29%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nail infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (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
Sepsis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (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
Hyponatraemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophosphataemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Rhabdomyosarcoma : Part 2		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 16 (43.75%)		
number of deaths (all causes)	3		
number of deaths resulting from			

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Rhabdomyosarcoma			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tumour associated fever			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tumour pain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombosis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Pain management			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			

subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral swelling				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Cough				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Haemothorax				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hypoxia				

subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Interstitial lung disease				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory distress				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Investigations				
Electrocardiogram abnormal				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Brain herniation				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			
Cardiac disorders				
Cardio-respiratory arrest				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			

Cardiopulmonary failure				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Left ventricular dysfunction				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Central nervous system haemorrhage				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coordination abnormal				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Drooling				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Generalised tonic-clonic seizure				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hemiparesis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Seizure				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Somnolence				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Salivary hypersecretion				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stomatitis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Vomiting			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rash			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Abscess			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bacteraemia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Clostridium difficile colitis			

subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nail infection				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pharyngitis				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii pneumonia				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperglycaemia				

subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hypophosphataemia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Temsirolimus 10mg/m2: Part 1	Temsirolimus 25mg/m2: Part 1	Temsirolimus 75mg/m2: Part 1
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	5 / 5 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neuroblastoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tumour pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypotension			

subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	3
Surgical and medical procedures			
Ear operation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nail operation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tooth repair			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Axillary pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Catheter site erythema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Catheter site rash			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Device occlusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Extravasation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Face oedema			

subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 4 (25.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Gait disturbance			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection site bruising			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	1 / 4 (25.00%)	1 / 5 (20.00%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Oedema peripheral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 5 (40.00%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ulcer			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	3
Reproductive system and breast disorders			

Pelvic pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bronchial obstruction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bronchospasm			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	2 / 4 (50.00%)	1 / 5 (20.00%)	1 / 3 (33.33%)
occurrences (all)	3	2	1
Dysphonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	1 / 4 (25.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Epistaxis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Hypoxia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lung infiltration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			

subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Pharyngeal erythema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pharyngeal inflammation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pneumonitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pneumothorax			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Pulmonary haemorrhage			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Rhinitis allergic			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Suffocation feeling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tachypnoea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Upper-airway cough syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			

Agitation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Attention deficit/hyperactivity disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Irritability			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mood altered			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	2 / 3 (66.67%)
occurrences (all)	1	0	16
Aspartate aminotransferase increased			

subjects affected / exposed	2 / 4 (50.00%)	2 / 5 (40.00%)	2 / 3 (66.67%)
occurrences (all)	3	3	10
Blood albumin decreased			
subjects affected / exposed	1 / 4 (25.00%)	1 / 5 (20.00%)	1 / 3 (33.33%)
occurrences (all)	1	2	6
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	4
Blood bicarbonate decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood calcium decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	6
Blood calcium increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood cholesterol increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	4
Blood creatinine increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Blood fibrinogen increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood glucose decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood glucose increased			
subjects affected / exposed	0 / 4 (0.00%)	2 / 5 (40.00%)	1 / 3 (33.33%)
occurrences (all)	0	3	9
Blood lactate dehydrogenase			

increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood magnesium decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Blood magnesium increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	4	0	1
Blood phosphorus decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	2 / 3 (66.67%)
occurrences (all)	0	7	14
Blood potassium decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	2 / 3 (66.67%)
occurrences (all)	0	4	9
Blood potassium increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood pressure decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood sodium decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Blood sodium increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Blood triglycerides increased			
subjects affected / exposed	1 / 4 (25.00%)	1 / 5 (20.00%)	2 / 3 (66.67%)
occurrences (all)	2	2	3
Blood urea increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac murmur			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	3 / 4 (75.00%)	0 / 5 (0.00%)	2 / 3 (66.67%)
occurrences (all)	5	0	13
High density lipoprotein decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Lipase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Low density lipoprotein increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	3 / 3 (100.00%)
occurrences (all)	0	7	11
Platelet count decreased			
subjects affected / exposed	1 / 4 (25.00%)	2 / 5 (40.00%)	2 / 3 (66.67%)
occurrences (all)	1	7	6
Weight decreased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Weight increased			

subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	1 / 4 (25.00%)	1 / 5 (20.00%)	3 / 3 (100.00%)
occurrences (all)	1	11	13
White blood cell count increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Arthropod bite			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	3
Contusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Head injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Humerus fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Radiation injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Sunburn			

subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Thermal burn			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Cardiac disorders			
Cyanosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Accessory nerve disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ataxia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cerebral haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyskinesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 4 (0.00%)	2 / 5 (40.00%)	1 / 3 (33.33%)
occurrences (all)	0	7	2
Hemiparesis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Partial seizures			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peripheral motor neuropathy			
subjects affected / exposed	1 / 4 (25.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Seizure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Spinal cord compression			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 4 (50.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	7	0	0

Leukopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	16
Neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Thrombocytopenia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	7	0	1
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
External ear disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
External ear pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Tympanic membrane perforation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Exophthalmos			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye disorder			

subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Eye pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Aphthous stomatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Breath odour			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chapped lips			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

Cheilitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Diarrhoea			
subjects affected / exposed	1 / 4 (25.00%)	1 / 5 (20.00%)	2 / 3 (66.67%)
occurrences (all)	1	2	3
Dyspepsia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eructation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Glossitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Haemorrhoids			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Lip dry			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Mouth ulceration			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	2 / 3 (66.67%)
occurrences (all)	0	1	4
Oesophageal pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	1 / 3 (33.33%)
occurrences (all)	0	4	2
Oral disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	1 / 4 (25.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	1	5	0
Periodontal disease			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Rectal discharge			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	1 / 4 (25.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Tooth impacted			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	3 / 4 (75.00%)	2 / 5 (40.00%)	1 / 3 (33.33%)
occurrences (all)	3	4	1
Hepatobiliary disorders			
Cholelithiasis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hepatomegaly			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Dermatitis acneiform			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis allergic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis diaper			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dry skin			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Ecchymosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Exfoliative rash			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Nail bed inflammation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nail bed tenderness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nail disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	5
Rash			
subjects affected / exposed	1 / 4 (25.00%)	1 / 5 (20.00%)	1 / 3 (33.33%)
occurrences (all)	1	2	2
Rash erythematous			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash follicular			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Scab			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin burning sensation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Glycosuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	3
Haematuria			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Haemoglobinuria			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Micturition disorder			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pollakiuria			
subjects affected / exposed	0 / 4 (0.00%)	2 / 5 (40.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Proteinuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urethral pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary tract disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urogenital haemorrhage			

subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Muscle twitching			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neck pain			

subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	1 / 4 (25.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Pain in jaw			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Infections and infestations			
Abscess			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Acne pustular			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Catheter site infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Cellulitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Clostridium difficile colitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	5
Conjunctivitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Device related infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fungal skin infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Furuncle			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Herpes simplex			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Lobar pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Localised infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Lung infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nail infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oesophageal candidiasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Osteomyelitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Otitis externa			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Parainfluenzae virus infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Pyoderma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Shunt infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Skin candida			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Staphylococcal infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 4 (25.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Acidosis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	2 / 4 (50.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	3	0	2
Dehydration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 5 (40.00%)	0 / 3 (0.00%)
occurrences (all)	0	12	0
Hyperglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Hypermagnesaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 5 (40.00%)	0 / 3 (0.00%)
occurrences (all)	0	9	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Hypocalcaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypochloraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			

subjects affected / exposed	2 / 4 (50.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	4
Hypoproteinaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Polydipsia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Temsirolimus 150mg/m2: Part 1	High-grade Glioma: Part 2	Neuroblastoma: Part 2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)	17 / 17 (100.00%)	19 / 19 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neuroblastoma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Tumour pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	4
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Haematoma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hypertension			

subjects affected / exposed	0 / 7 (0.00%)	3 / 17 (17.65%)	1 / 19 (5.26%)
occurrences (all)	0	4	1
Hypotension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Surgical and medical procedures			
Ear operation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	3	0
Nail operation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Tooth repair			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	3 / 19 (15.79%)
occurrences (all)	1	0	7
Axillary pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Catheter site erythema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Catheter site rash			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	1	0	2
Chest pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	2	0	2
Device occlusion			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Extravasation			

subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	4 / 7 (57.14%)	6 / 17 (35.29%)	6 / 19 (31.58%)
occurrences (all)	7	8	11
Gait disturbance			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Injection site bruising			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Mucosal inflammation			
subjects affected / exposed	2 / 7 (28.57%)	3 / 17 (17.65%)	0 / 19 (0.00%)
occurrences (all)	2	4	0
Oedema peripheral			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	3 / 19 (15.79%)
occurrences (all)	0	1	17
Pyrexia			
subjects affected / exposed	4 / 7 (57.14%)	1 / 17 (5.88%)	9 / 19 (47.37%)
occurrences (all)	6	1	29
Swelling			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Ulcer			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	1	0	2

Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Bronchial obstruction			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Bronchospasm			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	3
Cough			
subjects affected / exposed	3 / 7 (42.86%)	5 / 17 (29.41%)	6 / 19 (31.58%)
occurrences (all)	3	8	26
Dysphonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	0 / 7 (0.00%)	2 / 17 (11.76%)	3 / 19 (15.79%)
occurrences (all)	0	3	5
Epistaxis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	30
Hypoxia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	4
Lung infiltration			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			

subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	4 / 19 (21.05%)
occurrences (all)	0	0	8
Pharyngeal erythema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Pharyngeal inflammation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Pleural effusion			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Pneumonitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Pneumothorax			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pulmonary haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	1	0	10
Rhinorrhoea			
subjects affected / exposed	1 / 7 (14.29%)	1 / 17 (5.88%)	2 / 19 (10.53%)
occurrences (all)	3	1	9
Suffocation feeling			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	3
Tachypnoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Upper-airway cough syndrome			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Psychiatric disorders			

Agitation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Anxiety			
subjects affected / exposed	0 / 7 (0.00%)	2 / 17 (11.76%)	1 / 19 (5.26%)
occurrences (all)	0	3	2
Attention deficit/hyperactivity disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	3
Confusional state			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	1 / 7 (14.29%)	1 / 17 (5.88%)	1 / 19 (5.26%)
occurrences (all)	1	1	1
Irritability			
subjects affected / exposed	2 / 7 (28.57%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	5	0	2
Mood altered			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	1 / 19 (5.26%)
occurrences (all)	0	2	1
Sleep disorder			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	4	0	0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 7 (14.29%)	6 / 17 (35.29%)	7 / 19 (36.84%)
occurrences (all)	2	13	28
Aspartate aminotransferase increased			

subjects affected / exposed	2 / 7 (28.57%)	3 / 17 (17.65%)	6 / 19 (31.58%)
occurrences (all)	6	8	54
Blood albumin decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	4
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	4 / 19 (21.05%)
occurrences (all)	0	4	5
Blood bicarbonate decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	35
Blood bilirubin increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Blood calcium decreased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Blood calcium increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Blood cholesterol increased			
subjects affected / exposed	2 / 7 (28.57%)	3 / 17 (17.65%)	6 / 19 (31.58%)
occurrences (all)	3	9	16
Blood creatinine increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	3 / 19 (15.79%)
occurrences (all)	0	0	10
Blood fibrinogen increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	2
Blood glucose decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	4
Blood glucose increased			
subjects affected / exposed	2 / 7 (28.57%)	1 / 17 (5.88%)	4 / 19 (21.05%)
occurrences (all)	2	7	54
Blood lactate dehydrogenase			

increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Blood magnesium decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Blood magnesium increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	3 / 19 (15.79%)
occurrences (all)	0	0	15
Blood phosphorus decreased			
subjects affected / exposed	2 / 7 (28.57%)	1 / 17 (5.88%)	3 / 19 (15.79%)
occurrences (all)	9	1	10
Blood potassium decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	4 / 19 (21.05%)
occurrences (all)	0	0	19
Blood potassium increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	4
Blood pressure decreased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Blood sodium decreased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	2 / 19 (10.53%)
occurrences (all)	0	1	8
Blood sodium increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Blood triglycerides increased			
subjects affected / exposed	2 / 7 (28.57%)	4 / 17 (23.53%)	6 / 19 (31.58%)
occurrences (all)	4	20	66
Blood urea increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Cardiac murmur			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Haemoglobin decreased			
subjects affected / exposed	3 / 7 (42.86%)	1 / 17 (5.88%)	6 / 19 (31.58%)
occurrences (all)	6	2	60
High density lipoprotein decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	5
International normalised ratio increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Lipase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Low density lipoprotein increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Neutrophil count decreased			
subjects affected / exposed	3 / 7 (42.86%)	2 / 17 (11.76%)	4 / 19 (21.05%)
occurrences (all)	11	2	13
Platelet count decreased			
subjects affected / exposed	2 / 7 (28.57%)	4 / 17 (23.53%)	7 / 19 (36.84%)
occurrences (all)	4	10	24
Weight decreased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	2	0	2
Weight increased			

subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	5 / 7 (71.43%)	2 / 17 (11.76%)	6 / 19 (31.58%)
occurrences (all)	14	4	79
White blood cell count increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Arthropod bite			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Contusion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	9
Head injury			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Humerus fracture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Procedural pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Radiation injury			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Sunburn			

subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Thermal burn			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Cyanosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	3
Nervous system disorders			
Accessory nerve disorder			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Ataxia			
subjects affected / exposed	0 / 7 (0.00%)	2 / 17 (11.76%)	0 / 19 (0.00%)
occurrences (all)	0	3	0
Cerebral haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	1 / 7 (14.29%)	1 / 17 (5.88%)	1 / 19 (5.26%)
occurrences (all)	1	1	3
Dyskinesia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Headache			
subjects affected / exposed	3 / 7 (42.86%)	3 / 17 (17.65%)	4 / 19 (21.05%)
occurrences (all)	5	4	12
Hemiparesis			

subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Hyperaesthesia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Hypoaesthesia			
subjects affected / exposed	1 / 7 (14.29%)	2 / 17 (11.76%)	0 / 19 (0.00%)
occurrences (all)	1	2	0
Neuropathy peripheral			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Partial seizures			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	5
Peripheral motor neuropathy			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	3	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	1 / 19 (5.26%)
occurrences (all)	0	1	4
Seizure			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Spinal cord compression			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 7 (42.86%)	0 / 17 (0.00%)	5 / 19 (26.32%)
occurrences (all)	12	0	73

Leukopenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	4 / 19 (21.05%)
occurrences (all)	0	0	27
Lymphopenia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	2 / 19 (10.53%)
occurrences (all)	0	1	10
Neutropenia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	3 / 19 (15.79%)
occurrences (all)	1	0	79
Thrombocytopenia			
subjects affected / exposed	2 / 7 (28.57%)	5 / 17 (29.41%)	6 / 19 (31.58%)
occurrences (all)	12	11	37
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Ear pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	2	0	2
External ear disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	5
External ear pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Tympanic membrane perforation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	4	0
Vertigo			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Exophthalmos			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Eye disorder			

subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Eye pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Lacrimation increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Periorbital oedema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Visual acuity reduced			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	6 / 19 (31.58%)
occurrences (all)	0	1	16
Abdominal pain upper			
subjects affected / exposed	1 / 7 (14.29%)	2 / 17 (11.76%)	0 / 19 (0.00%)
occurrences (all)	1	2	0
Aphthous stomatitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Breath odour			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Chapped lips			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Cheilitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	2 / 7 (28.57%)	1 / 17 (5.88%)	5 / 19 (26.32%)
occurrences (all)	3	1	7
Diarrhoea			
subjects affected / exposed	2 / 7 (28.57%)	3 / 17 (17.65%)	2 / 19 (10.53%)
occurrences (all)	5	3	5
Dyspepsia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Dysphagia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Eructation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Flatulence			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Gingival bleeding			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Glossitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Haemorrhoids			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Lip dry			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	1	0

Mouth ulceration			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	4 / 7 (57.14%)	1 / 17 (5.88%)	4 / 19 (21.05%)
occurrences (all)	7	2	12
Oesophageal pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	4	0	2
Oral disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Periodontal disease			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Rectal discharge			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	1 / 7 (14.29%)	2 / 17 (11.76%)	5 / 19 (26.32%)
occurrences (all)	1	2	7
Tooth impacted			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	2 / 7 (28.57%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Vomiting			
subjects affected / exposed	4 / 7 (57.14%)	5 / 17 (29.41%)	2 / 19 (10.53%)
occurrences (all)	5	7	5
Hepatobiliary disorders			
Cholelithiasis			

subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hepatomegaly			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Hyperbilirubinaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 7 (14.29%)	2 / 17 (11.76%)	0 / 19 (0.00%)
occurrences (all)	1	3	0
Alopecia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	2	0	2
Dermatitis acneiform			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	3	0
Dermatitis allergic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Dermatitis diaper			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Dry skin			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	3 / 19 (15.79%)
occurrences (all)	0	1	6
Ecchymosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Exfoliative rash			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	3	0	1
Hyperhidrosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Nail bed inflammation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Nail bed tenderness			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Nail disorder			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	2 / 19 (10.53%)
occurrences (all)	0	1	2
Pruritus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	3 / 19 (15.79%)
occurrences (all)	0	0	7
Rash			
subjects affected / exposed	4 / 7 (57.14%)	5 / 17 (29.41%)	3 / 19 (15.79%)
occurrences (all)	5	10	7
Rash erythematous			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Rash follicular			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Rash pruritic			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Scab			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Skin burning sensation			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Skin disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Skin lesion			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	1 / 19 (5.26%)
occurrences (all)	0	1	1

Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Dysuria			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Glycosuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Haematuria			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Haemoglobinuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Micturition disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	3 / 19 (15.79%)
occurrences (all)	0	0	8
Urethral pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Urinary retention			
subjects affected / exposed	0 / 7 (0.00%)	2 / 17 (11.76%)	1 / 19 (5.26%)
occurrences (all)	0	3	1
Urinary tract disorder			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Urogenital haemorrhage			

subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 7 (14.29%)	2 / 17 (11.76%)	6 / 19 (31.58%)
occurrences (all)	2	2	12
Back pain			
subjects affected / exposed	2 / 7 (28.57%)	2 / 17 (11.76%)	4 / 19 (21.05%)
occurrences (all)	7	2	6
Bone pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	3
Muscle spasms			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	2 / 19 (10.53%)
occurrences (all)	0	1	3
Muscle twitching			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Muscular weakness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	3
Musculoskeletal chest pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 7 (14.29%)	1 / 17 (5.88%)	2 / 19 (10.53%)
occurrences (all)	1	1	3
Myalgia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Neck pain			

subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	3
Pain in extremity			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	5 / 19 (26.32%)
occurrences (all)	0	1	18
Pain in jaw			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Infections and infestations			
Abscess			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	3	0
Acne pustular			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	6
Candida infection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Catheter site infection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Cellulitis			
subjects affected / exposed	0 / 7 (0.00%)	2 / 17 (11.76%)	0 / 19 (0.00%)
occurrences (all)	0	7	0
Clostridium difficile colitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	3 / 19 (15.79%)
occurrences (all)	0	0	6
Cystitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Device related infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Ear infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	1 / 19 (5.26%)
occurrences (all)	0	2	1
Folliculitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Fungal skin infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Furuncle			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 7 (0.00%)	2 / 17 (11.76%)	1 / 19 (5.26%)
occurrences (all)	0	2	1
Gingivitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Herpes simplex			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Laryngitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Lobar pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Localised infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2

Lung infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Nail infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	5
Nasopharyngitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	3
Oesophageal candidiasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	0 / 7 (0.00%)	3 / 17 (17.65%)	1 / 19 (5.26%)
occurrences (all)	0	3	1
Oral herpes			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	3
Osteomyelitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	3
Otitis externa			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	7
Parainfluenzae virus infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Paronychia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	1 / 19 (5.26%)
occurrences (all)	0	1	10
Pharyngitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	3

Pyoderma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	4 / 19 (21.05%)
occurrences (all)	0	0	8
Shunt infection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	6
Skin candida			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Staphylococcal infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	3 / 17 (17.65%)	5 / 19 (26.32%)
occurrences (all)	0	4	18
Urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)	2 / 17 (11.76%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Viral infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Acidosis			

subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	6 / 7 (85.71%)	3 / 17 (17.65%)	6 / 19 (31.58%)
occurrences (all)	8	5	11
Dehydration			
subjects affected / exposed	1 / 7 (14.29%)	1 / 17 (5.88%)	1 / 19 (5.26%)
occurrences (all)	1	4	1
Hypercalcaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Hypercholesterolaemia			
subjects affected / exposed	2 / 7 (28.57%)	3 / 17 (17.65%)	2 / 19 (10.53%)
occurrences (all)	7	5	10
Hyperglycaemia			
subjects affected / exposed	2 / 7 (28.57%)	2 / 17 (11.76%)	2 / 19 (10.53%)
occurrences (all)	4	6	32
Hypermagnesaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Hypertriglyceridaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	13
Hypoalbuminaemia			
subjects affected / exposed	4 / 7 (57.14%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	11	0	2
Hypocalcaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	37
Hypochloraemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	29
Hypoglycaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 17 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	28
Hypokalaemia			

subjects affected / exposed	3 / 7 (42.86%)	1 / 17 (5.88%)	4 / 19 (21.05%)
occurrences (all)	7	2	15
Hypomagnesaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Hyponatraemia			
subjects affected / exposed	3 / 7 (42.86%)	0 / 17 (0.00%)	2 / 19 (10.53%)
occurrences (all)	6	0	6
Hypophosphataemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	6 / 19 (31.58%)
occurrences (all)	0	0	33
Hypoproteinaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 17 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Polydipsia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 17 (5.88%)	0 / 19 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Rhabdomyosarcoma : Part 2		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 16 (93.75%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neuroblastoma			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Tumour pain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Haematoma			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hypertension			

subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Hypotension			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Surgical and medical procedures			
Ear operation			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Nail operation			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Tooth repair			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Axillary pain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Catheter site erythema			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Catheter site rash			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Device occlusion			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Extravasation			

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Face oedema			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	5 / 16 (31.25%)		
occurrences (all)	10		
Gait disturbance			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Injection site bruising			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Mucosal inflammation			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	3		
Oedema peripheral			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Pain			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Pyrexia			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	5		
Swelling			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Ulcer			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		

Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Bronchial obstruction			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Bronchospasm			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	7		
Dysphonia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	6		
Epistaxis			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	3		
Hypoxia			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Lung infiltration			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Nasal congestion			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Pharyngeal erythema			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Pharyngeal inflammation			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Pleural effusion			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Pneumonitis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Pneumothorax			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Pulmonary haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Rhinitis allergic			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	3		
Suffocation feeling			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Tachypnoea			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Upper-airway cough syndrome			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			

Agitation			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Anxiety			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	4		
Attention deficit/hyperactivity disorder			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Confusional state			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Irritability			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Mood altered			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Sleep disorder			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Alanine aminotransferase increased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Aspartate aminotransferase increased			

subjects affected / exposed	5 / 16 (31.25%)			
occurrences (all)	6			
Blood albumin decreased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Blood alkaline phosphatase increased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Blood bicarbonate decreased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	2			
Blood bilirubin increased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Blood calcium decreased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Blood calcium increased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Blood cholesterol increased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	2			
Blood creatinine increased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Blood fibrinogen increased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Blood glucose decreased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Blood glucose increased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Blood lactate dehydrogenase				

increased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Blood magnesium decreased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Blood magnesium increased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	2			
Blood phosphorus decreased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Blood potassium decreased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Blood potassium increased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Blood pressure decreased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Blood sodium decreased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Blood sodium increased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Blood triglycerides increased				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences (all)	5			
Blood urea increased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Cardiac murmur				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			

Electrocardiogram QT prolonged				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	2			
Gamma-glutamyltransferase increased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Glycosylated haemoglobin increased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Haemoglobin decreased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
High density lipoprotein decreased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
International normalised ratio increased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Lipase increased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Low density lipoprotein increased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Neutrophil count decreased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Platelet count decreased				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences (all)	2			
Weight decreased				
subjects affected / exposed	3 / 16 (18.75%)			
occurrences (all)	4			
Weight increased				

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
White blood cell count decreased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
White blood cell count increased			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Arthropod bite			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Head injury			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Humerus fracture			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Procedural pain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Radiation injury			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Skin abrasion			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Sunburn			

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Thermal burn			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Cyanosis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Pericardial effusion			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	4		
Nervous system disorders			
Accessory nerve disorder			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Ataxia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Cerebral haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Dyskinesia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	10		
Hemiparesis			

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hyperaesthesia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hypoaesthesia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	4		
Neuropathy peripheral			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Partial seizures			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Peripheral motor neuropathy			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Seizure			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Spinal cord compression			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Syncope			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	4		

Leukopenia			
subjects affected / exposed	5 / 16 (31.25%)		
occurrences (all)	12		
Lymphopenia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	3		
Neutropenia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Thrombocytopenia			
subjects affected / exposed	6 / 16 (37.50%)		
occurrences (all)	16		
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Ear pain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
External ear disorder			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
External ear pain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Tympanic membrane perforation			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Vertigo			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Eye disorders			
Exophthalmos			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Eye disorder			

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Eye pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Lacrimation increased			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Ocular hyperaemia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Periorbital oedema			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Visual acuity reduced			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	3		
Abdominal pain upper			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Aphthous stomatitis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Breath odour			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Chapped lips			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		

Cheilitis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Constipation				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Diarrhoea				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Dyspepsia				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Dysphagia				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Eructation				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Flatulence				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Gastrointestinal pain				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Gingival bleeding				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Glossitis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Haemorrhoids				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Lip dry				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			

Mouth ulceration subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Nausea subjects affected / exposed occurrences (all)	4 / 16 (25.00%) 4		
Oesophageal pain subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 2		
Oral disorder subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Oral pain subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Periodontal disease subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Rectal discharge subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Stomatitis subjects affected / exposed occurrences (all)	3 / 16 (18.75%) 12		
Tooth impacted subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Toothache subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Vomiting subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Hepatobiliary disorders Cholelithiasis			

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hepatomegaly			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hyperbilirubinaemia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	3		
Alopecia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Dermatitis acneiform			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Dermatitis allergic			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Dermatitis diaper			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	3		
Ecchymosis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Exfoliative rash			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hyperhidrosis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		

Nail bed inflammation				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Nail bed tenderness				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Nail disorder				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Pruritus				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Rash				
subjects affected / exposed	3 / 16 (18.75%)			
occurrences (all)	3			
Rash erythematous				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Rash follicular				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Rash pruritic				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Scab				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Skin burning sensation				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Skin disorder				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Skin lesion				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			

Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Dysuria			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Glycosuria			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Haematuria			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Haemoglobinuria			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Micturition disorder			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Pollakiuria			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Proteinuria			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Urethral pain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Urinary retention			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Urinary tract disorder			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Urogenital haemorrhage			

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	4		
Back pain			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	5		
Bone pain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Muscle twitching			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Muscular weakness			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	5		
Myalgia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Neck pain			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Pain in jaw			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Abscess			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Acne pustular			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	5		
Bronchitis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Candida infection			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Catheter site infection			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Cellulitis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Clostridium difficile colitis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Conjunctivitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Cystitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		

Device related infection				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Ear infection				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	2			
Folliculitis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Fungal skin infection				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Furuncle				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Gastroenteritis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Gingivitis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Herpes simplex				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Infection				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	2			
Laryngitis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Lobar pneumonia				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Localised infection				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			

Lung infection				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Nail infection				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Nasopharyngitis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Oesophageal candidiasis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Oral candidiasis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Oral herpes				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Osteomyelitis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Otitis externa				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Parainfluenzae virus infection				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Paronychia				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Pharyngitis				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences (all)	5			
Pneumonia				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			

Pyoderma subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 4		
Respiratory syncytial virus infection subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Rhinitis subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Shunt infection subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Sinusitis subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Skin candida subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Staphylococcal infection subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Tooth infection subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 16 (18.75%) 4		
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Viral infection subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Metabolism and nutrition disorders Acidosis			

subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Decreased appetite				
subjects affected / exposed	6 / 16 (37.50%)			
occurrences (all)	8			
Dehydration				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Hypercalcaemia				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	2			
Hypercholesterolaemia				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Hyperglycaemia				
subjects affected / exposed	3 / 16 (18.75%)			
occurrences (all)	7			
Hypermagnesaemia				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Hypertriglyceridaemia				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences (all)	3			
Hypoalbuminaemia				
subjects affected / exposed	3 / 16 (18.75%)			
occurrences (all)	3			
Hypocalcaemia				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	3			
Hypochloraemia				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Hypoglycaemia				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	3			
Hypokalaemia				

subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	4		
Hypomagnesaemia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hyponatraemia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hypophosphataemia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hypoproteinaemia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Polydipsia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 May 2005	Protocol amendment included concomitment medications.
08 May 2006	It was done to clarify inclusion criteria for pancreatic cancer and bring disease assessment in line with the progression assessment endpoint timing.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported