Clinical trial results:
A Phase 2 clinical study of pomalidomide (CC-4047) monotherapy for children and young adults with recurrent or progressive primary brain tumors.

Summary

EudraCT number	2016-002903-25
Trial protocol	ES FR GB IT
Global end of trial date	14 September 2023

Results information

Result version number	v1 (current)
This version publication date	24 March 2024
First version publication date	24 March 2024

Trial information

Trial identification

Sponsor protocol code	CC-4047-BRN-001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.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	19 October 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 September 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Establish the preliminary efficacy of pomalidomide in children and young adults with recurrent or progressive primary brain tumors within four distinct tumor types.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 September 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 20
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	United States: 12
Worldwide total number of subjects	53
EEA total number of subjects	32

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	26
Adolescents (12-17 years)	27
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study consisted of 4 groups, for each of the following primary brain tumor types: diffuse intrinsic pontine glioma (DIPG), ependymoma, high-grade glioma, and medulloblastoma.

Pre-assignment

Screening details:

In stage 1 approximately 9 participants were to be enrolled in parallel to each group. If two or more participants in a group achieved an objective response or long-term stable disease within the first 6 cycles of treatment (within the first 3 cycles for DIPG) an additional 11 participants were to be enrolled in that group.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Diffuse Intrinsic Pontine Glioma

Arm description:

Participants received 2.6 mg/m²/day oral pomalidomide on days 1 to 21 of each 28-day treatment cycle for up to 24 cycles or until disease progression, withdrawal of consent/assent, treatment became intolerable, or death, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	pomalidomide
Investigational medicinal product code	CC-4047
Other name	
Pharmaceutical forms	Capsule, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

2.6 mg/m²/day

Arm title	Ependymoma

Arm description:

Participants received 2.6 mg/m²/day oral pomalidomide on days 1 to 21 of each 28-day treatment cycle for up to 24 cycles or until disease progression, withdrawal of consent/assent, treatment became intolerable, or death, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	pomalidomide
Investigational medicinal product code	CC-4047
Other name	
Pharmaceutical forms	Capsule, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

2.6 mg/m²/day

Arm title	High-grade Glioma

Arm description:

Participants received 2.6 mg/m²/day oral pomalidomide on days 1 to 21 of each 28-day treatment cycle for up to 24 cycles or until disease progression, withdrawal of consent/assent, treatment became intolerable, or death, whichever occurred first.

Arm type	Experimental

Investigational medicinal product name	pomalidomide
Investigational medicinal product code	CC-4047
Other name	
Pharmaceutical forms	Capsule, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

2.6 mg/m²/day

Arm title	Medulloblastoma

Arm description:

Participants received 2.6 mg/m²/day oral pomalidomide on days 1 to 21 of each 28-day treatment cycle for up to 24 cycles or until disease progression, withdrawal of consent/assent, treatment became intolerable, or death, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	pomalidomide
Investigational medicinal product code	CC-4047
Other name	
Pharmaceutical forms	Capsule, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

2.6 mg/m²/day

Number of subjects in period 1	Diffuse Intrinsic Pontine Glioma	Ependymoma	High-grade Glioma
Started	11	9	23
Received Study Drug	11	9	22
Completed	0	0	1
Not completed	11	9	22
Adverse event, serious fatal	1	-	1
Adverse event, non-fatal	-	-	2
Progressive Disease	10	9	17
Withdrawal by Parent/Guardian	-	-	2

Number of subjects in period 1	Medulloblastoma
Started	10
Received Study Drug	10
Completed	0
Not completed	10
Adverse event, serious fatal	1
Adverse event, non-fatal	-
Progressive Disease	8
Withdrawal by Parent/Guardian	1

Baseline characteristics

Reporting groups	
Reporting group title	Diffuse Intrinsic Pontine Glioma
Reporting group description:	
Participants received 2.6 mg/m²/day oral pomalidomide on days 1 to 21 of each 28-day treatment cycle for up to 24 cycles or until disease progression, withdrawal of consent/assent, treatment became intolerable, or death, whichever occurred first.	
Reporting group title	Ependymoma
Reporting group description:	
Participants received 2.6 mg/m²/day oral pomalidomide on days 1 to 21 of each 28-day treatment cycle for up to 24 cycles or until disease progression, withdrawal of consent/assent, treatment became intolerable, or death, whichever occurred first.	
Reporting group title	High-grade Glioma
Reporting group description:	
Participants received 2.6 mg/m²/day oral pomalidomide on days 1 to 21 of each 28-day treatment cycle for up to 24 cycles or until disease progression, withdrawal of consent/assent, treatment became intolerable, or death, whichever occurred first.	
Reporting group title	Medulloblastoma
Reporting group description:	
Participants received 2.6 mg/m²/day oral pomalidomide on days 1 to 21 of each 28-day treatment cycle for up to 24 cycles or until disease progression, withdrawal of consent/assent, treatment became intolerable, or death, whichever occurred first.	

Reporting group values	Diffuse Intrinsic Pontine Glioma	Ependymoma	High-grade Glioma
Number of subjects	11	9	23
Age Categorical Units: participants			
≥ 1 to < 6 years	1	2	1
≥ 6 to < 12 years	9	1	5
≥ 12 years	1	6	17
Age Continuous Units: years			
median	7.0	12.0	14.0
full range (min-max)	4 to 12	4 to 15	5 to 18
Sex: Female, Male Units: participants			
Female	4	4	8
Male	7	5	15
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	4	0	6
Not Hispanic or Latino	7	9	13
Unknown or Not Reported	0	0	4
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaskan Native	0	0	0
Asian	1	0	2
Black or African American	0	0	2
Native Hawaiian or Other Pacific Islander	0	0	0

White	10	9	11
Not Collected or Reported	0	0	5
Other	0	0	3

Reporting group values	Medulloblastoma	Total	
Number of subjects	10	53	
Age Categorical Units: participants			
≥ 1 to < 6 years	1	5	
≥ 6 to < 12 years	6	21	
≥ 12 years	3	27	
Age Continuous Units: years			
median	10.0		
full range (min-max)	4 to 17	-	
Sex: Female, Male Units: participants			
Female	3	19	
Male	7	34	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	11	
Not Hispanic or Latino	8	37	
Unknown or Not Reported	1	5	
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaskan Native	0	0	
Asian	0	3	
Black or African American	0	2	
Native Hawaiian or Other Pacific Islander	0	0	
White	8	38	
Not Collected or Reported	2	7	
Other	0	3	

End points

End points reporting groups

Reporting group title	Diffuse Intrinsic Pontine Glioma
Reporting group description:	
Participants received 2.6 mg/m²/day oral pomalidomide on days 1 to 21 of each 28-day treatment cycle for up to 24 cycles or until disease progression, withdrawal of consent/assent, treatment became intolerable, or death, whichever occurred first.	
Reporting group title	Ependymoma
Reporting group description:	
Participants received 2.6 mg/m²/day oral pomalidomide on days 1 to 21 of each 28-day treatment cycle for up to 24 cycles or until disease progression, withdrawal of consent/assent, treatment became intolerable, or death, whichever occurred first.	
Reporting group title	High-grade Glioma
Reporting group description:	
Participants received 2.6 mg/m²/day oral pomalidomide on days 1 to 21 of each 28-day treatment cycle for up to 24 cycles or until disease progression, withdrawal of consent/assent, treatment became intolerable, or death, whichever occurred first.	
Reporting group title	Medulloblastoma
Reporting group description:	
Participants received 2.6 mg/m²/day oral pomalidomide on days 1 to 21 of each 28-day treatment cycle for up to 24 cycles or until disease progression, withdrawal of consent/assent, treatment became intolerable, or death, whichever occurred first.	

Primary: Percentage of Participants with an Objective Response and Long-term Stable Disease

End point title	Percentage of Participants with an Objective Response and Long-term Stable Disease[1]
End point description:	
The percentage of participants who achieved either an objective response, defined as a complete response (CR) or partial response (PR) in the first 6 cycles of treatment (or within 3 cycles for DIPG), or long-term stable disease (SD) defined as SD maintained for ≥ 6 cycles (≥ 3 cycles for DIPG), measured from first dose date. CR: Disappearance of all lesions and no new lesions. PR: A reduction of ≥ 50% in the size of measurable lesions, and/or persistence of non-target lesions with no progression or decrease in size. SD: A decrease of < 50% or an increase of < 25% in the size of measurable lesions and no evidence of new lesions, response does not meet the criteria for CR, PR, or progressive disease, and/or the persistence of non-target lesions with no progression or decrease in size. Progressive Disease (PD): ≥ 25% increase in the size of the measurable lesions, or the appearance of one or more new lesions and/or unequivocal progression of existing non-target lesions.	
End point type	Primary
End point timeframe:	
6 months (first 6 cycles) or 3 months (first 3 cycles) for participants in the DIPG group	
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 summary statistics planned for this endpoint.	

End point values	Diffuse Intrinsic Pontine Glioma	Ependymoma	High-grade Glioma	Medulloblastoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	9	19	9
Units: percentage of participants				
number (confidence interval 95%)	0 (0.0 to 33.6)	11.1 (0.3 to 48.2)	10.5 (1.3 to 33.1)	0 (0.0 to 33.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieved an Objective Response (ORR)

End point title	Percentage of Participants who Achieved an Objective Response (ORR)

End point description:

Objective response rate was defined as the percentage of participants who achieved a complete response (CR) or partial response (PR) within the first 6 cycles of treatment (or within 3 cycles for participants in the DIPG group). Disease assessments were based on MRI and assessed by an independent central review. CR: Disappearance of all lesions and no new lesions. PR: A reduction of ≥ 50% in the size of measurable lesions compared to baseline, and/or the persistence of non-target lesions with no progression or decrease in size. Progressive Disease (PD): ≥ 25% increase in the size of the measurable lesions, or the appearance of one or more new lesions and/or unequivocal progression of existing non-target lesions.

End point type	Secondary

End point timeframe:

6 months (first 6 cycles) or 3 months (first 3 cycles) for participants in the DIPG group

End point values	Diffuse Intrinsic Pontine Glioma	Ependymoma	High-grade Glioma	Medulloblastoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	9	19	9
Units: percentage of participants				
number (confidence interval 95%)	0 (0.0 to 33.6)	0 (0.0 to 33.6)	5.3 (0.1 to 26.0)	0 (0.0 to 33.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Long-term Stable Disease

End point title	Percentage of Participants with Long-term Stable Disease

End point description:

Long-term stable disease (SD) rate was defined as the percentage of participants who achieved SD maintained for ≥ 6 cycles (or > 3 cycles for DIPG), measured from the date of first dose of treatment. Disease assessments were based on MRI and assessed by an independent central review. SD: A decrease of < 50% or an increase of < 25% in the size of measurable lesions and no evidence of new lesions, response does not meet the criteria for CR, PR, or progressive disease, and/or the persistence of non-target lesions with no progression or decrease in size. CR: Disappearance of all lesions and no new lesions. PR: A reduction of ≥ 50% in the size of measurable lesions compared to baseline, and/or the persistence of non-target lesions with no progression or decrease in size. Progressive Disease (PD): ≥ 25% increase in the size of the measurable lesions, or the appearance of one or more new lesions

and/or unequivocal progression of existing non-target lesions.

End point type	Secondary

End point timeframe:

6 months (first 6 cycles) or 3 months (first 3 cycles) for participants in the DIPG group

End point values	Diffuse Intrinsic Pontine Glioma	Ependymoma	High-grade Glioma	Medulloblastoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	9	19	9
Units: percentage of participants				
number (confidence interval 95%)	0 (0.0 to 33.6)	11.1 (0.3 to 48.2)	5.3 (0.1 to 26.0)	0 (0.0 to 33.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of Duration of Response (DoR)

End point title	Kaplan-Meier Estimate of Duration of Response (DoR)

End point description:

DoR is defined as the time from the date of the first objective response (complete response [CR] or partial response [PR]) to disease progression. Participants who did not have disease progression or had not died were censored at the time of their last disease assessment or at the time of start of new anticancer therapy, whichever occurred first. Progressive disease (PD): ≥ 25% increase in the size of the measurable lesions taking as a reference the smallest disease measurement recorded since the start of protocol therapy (nadir), or the appearance of one or more new lesions and/or unequivocal progression of existing non-target lesions, or if spine MRI and/or lumbar cerebrospinal fluid (CSF) cytology were previously negative and became positive. CR: Disappearance of all lesions and no new lesions. PR: A reduction of ≥ 50% in the size of measurable lesions compared to baseline, and/or the persistence of non-target lesions with no progression or decrease in size.
-99999, 99999 = NA

End point type	Secondary

End point timeframe:

From the first dose of pomalidomide to the date of the first documented tumor progression or death due to any cause, whichever occurs first (Up to 71 months)

End point values	Diffuse Intrinsic Pontine Glioma	Ependymoma	High-grade Glioma	Medulloblastoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	0[2]	1	0[3]
Units: weeks				
median (confidence interval 95%)	12.29 (-99999 to 99999)	(to)	99999 (99999 to 99999)	(to)

Notes:

[2] - 0 participants with CR or PR

[3] - 0 participants with CR or PR

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of Progression-Free Survival (PFS)

End point title	Kaplan-Meier Estimate of Progression-Free Survival (PFS)

End point description:

Progression-free survival was defined as the time from the date of first dose of pomalidomide until the date progressive disease (PD) was first observed or until the date of death due to any cause, whichever occurred first. Participants who did not have PD or had not died at the time of analysis were censored at the time of their last disease assessment or at the start of new anticancer therapy, whichever occurred first. Progressive Disease (PD): ≥ 25% increase in the size of the measurable lesions taking as a reference the smallest disease measurement recorded since the start of protocol therapy (nadir), or the appearance of one or more new lesions and/or unequivocal progression of existing non-target lesions, or if spine MRI and/or lumbar CSF cytology were previously negative and became positive.

End point type	Secondary

End point timeframe:

From the first dose of pomalidomide to the date of the first documented tumor progression or death due to any cause, whichever occurs first (Up to 71 months)

End point values	Diffuse Intrinsic Pontine Glioma	Ependymoma	High-grade Glioma	Medulloblastoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	9	23	10
Units: weeks				
median (confidence interval 95%)	11.43 (4.43 to 12.57)	8.43 (5.57 to 16.14)	7.86 (5.43 to 8.29)	8.29 (7.29 to 18.00)

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of Overall Survival (OS)

End point title	Kaplan-Meier Estimate of Overall Survival (OS)

End point description:

Overall survival was defined as the time from the date of the first dose to the date of death (any cause). Participants who were alive were censored at the last known time that the participant was alive.

End point type	Secondary

End point timeframe:

From the first dose of pomalidomide to the date of death due to any cause (Up to 71 months)

End point values	Diffuse Intrinsic Pontine Glioma	Ependymoma	High-grade Glioma	Medulloblastoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	9	23	10
Units: months				
median (confidence interval 95%)	4.86 (1.02 to 10.91)	12.02 (2.86 to 20.90)	5.06 (2.04 to 16.66)	11.60 (1.74 to 35.32)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment-Emergent Adverse Events (TEAEs)

End point title	Number of Participants with Treatment-Emergent Adverse Events (TEAEs)

End point description:

Treatment-emergent adverse events were defined as any adverse events (AE) occurring from the first dose of pomalidomide until 28 days after the last dose. The severity of each AE was graded according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE), Version 4.03 and according to the following scale: Grade 1: Mild (transient or mild discomfort; no limitation in activity or medical intervention required); Grade 2: Moderate (mild to moderate limitation in activity, assistance may be needed; minimal medical intervention required); Grade 3: Severe (marked limitation in activity, assistance and medical intervention required, hospitalization possible); Grade 4: Life-threatening (extreme limitation in activity, significant assistance or medical intervention required, hospitalization or hospice care probable); Grade 5: Death. Drug-related AEs are those suspected by the Investigator as being related to administration of study drug.

End point type	Secondary

End point timeframe:

From the first dose of pomalidomide until 28 days after the last dose (Up to approximately 72 months)

End point values	Diffuse Intrinsic Pontine Glioma	Ependymoma	High-grade Glioma	Medulloblastoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	9	22	10
Units: participants				
Any treatment-emergent adverse event (TEAE)	11	8	21	9
TEAE related to study drug	5	7	14	8
Serious TEAE	9	4	14	4
Serious TEAE related to study drug	1	0	6	0
Grade 3/4 TEAE	8	6	14	6
Grade 3/4 TEAE related to study drug	3	2	10	4
TEAE leading to death	5	1	3	1
TEAE leading to dose reduction	1	0	3	0

TEAE leading to dose interruption	4	3	5	2
TEAE leading to study drug discontinuation	2	1	2	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Participants were assessed for all-cause mortality from their first dose until their study completion (up to approximately 72 months). SAEs and other AEs were assessed from first dose until 28 days after last dose (up to approximately 72 months).

Adverse event reporting additional description:

The number at Risk for All-cause mortality represents all enrolled participants, regardless of whether the participant received study treatment or not. The number at Risk for Serious Adverse Events and Other (Not Including Serious) Adverse Events represents all participants who received at least 1 dose of pomalidomide.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Diffuse Intrinsic Pontine Glioma

Reporting group description:

Participants received 2.6 mg/m²/day oral pomalidomide on days 1 to 21 of each 28-day treatment cycle for up to 24 cycles or until disease progression, withdrawal of consent/assent, treatment became intolerable, or death, whichever occurred first.

Reporting group title	Ependymoma

Reporting group description:

Participants received 2.6 mg/m²/day oral pomalidomide on days 1 to 21 of each 28-day treatment cycle for up to 24 cycles or until disease progression, withdrawal of consent/assent, treatment became intolerable, or death, whichever occurred first.

Reporting group title	High-grade Glioma

Reporting group description:

Participants received 2.6 mg/m²/day oral pomalidomide on days 1 to 21 of each 28-day treatment cycle for up to 24 cycles or until disease progression, withdrawal of consent/assent, treatment became intolerable, or death, whichever occurred first.

Reporting group title	Medulloblastoma

Reporting group description:

Participants received 2.6 mg/m²/day oral pomalidomide on days 1 to 21 of each 28-day treatment cycle for up to 24 cycles or until disease progression, withdrawal of consent/assent, treatment became intolerable, or death, whichever occurred first.

Serious adverse events	Diffuse Intrinsic Pontine Glioma	Ependymoma	High-grade Glioma
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 11 (81.82%)	4 / 9 (44.44%)	14 / 22 (63.64%)
number of deaths (all causes)	11	6	15
number of deaths resulting from adverse events	5	1	3
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			

subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Hydrocephalus			
subjects affected / exposed	0 / 11 (0.00%)	2 / 9 (22.22%)	2 / 22 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	3 / 22 (13.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 11 (9.09%)	2 / 9 (22.22%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyskinesia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depressed level of consciousness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ataxia			

subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial pressure increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Monoplegia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (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 / 11 (0.00%)	0 / 9 (0.00%)	2 / 22 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (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
Paraesthesia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurological decompensation			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Dysmetria			

subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (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
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Gait disturbance			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 22 (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
Malaise			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	2 / 11 (18.18%)	1 / 9 (11.11%)	2 / 22 (9.09%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 2
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumonitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (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
Dyspnoea			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Infections and infestations			
Respiratory syncytial virus bronchitis			

subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (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
Pneumonia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	2 / 22 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mastoiditis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (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
Anorectal infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Medulloblastoma		

Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 10 (40.00%)		
number of deaths (all causes)	9		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Hydrocephalus			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hemiparesis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	0 / 10 (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 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyskinesia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Depressed level of consciousness				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ataxia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intracranial pressure increased				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Monoplegia				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Presyncope				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Paraesthesia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neurological decompensation				

subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dysmetria				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Neutropenia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Gait disturbance				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malaise				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			

Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Respiratory syncytial virus bronchitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mastoiditis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Herpes zoster			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Encephalitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anorectal infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			

Hyponatraemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Diffuse Intrinsic Pontine Glioma	Ependymoma	High-grade Glioma
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 11 (100.00%)	8 / 9 (88.89%)	20 / 22 (90.91%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Pallor			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Gait disturbance			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	2 / 11 (18.18%)	1 / 9 (11.11%)	4 / 22 (18.18%)
occurrences (all)	2	1	4
Asthenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	3 / 22 (13.64%)
occurrences (all)	0	0	3
General physical health deterioration			

subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	2 / 11 (18.18%)	1 / 9 (11.11%)	2 / 22 (9.09%)
occurrences (all)	2	1	2
Oedema peripheral			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Non-cardiac chest pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Bronchostenosis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	3 / 22 (13.64%)
occurrences (all)	1	0	5
Tonsillar inflammation			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Dyspnoea			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Hiccups			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Hypoxia			

subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Pharyngeal erythema			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Respiratory failure			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Personality change			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Confusional state			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	1 / 22 (4.55%)
occurrences (all)	0	2	1
Investigations			
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 22 (0.00%)
occurrences (all)	0	2	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 11 (9.09%)	1 / 9 (11.11%)	4 / 22 (18.18%)
occurrences (all)	1	2	4
Urine output decreased			

subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Injury, poisoning and procedural complications			
Upper limb fracture			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Ligament sprain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Fall			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Contusion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 11 (27.27%)	4 / 9 (44.44%)	5 / 22 (22.73%)
occurrences (all)	5	7	14
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Depressed level of consciousness			

subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Ataxia			
subjects affected / exposed	2 / 11 (18.18%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences (all)	2	0	1
Aphasia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Hemiparesis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Hydrocephalus			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Muscle spasticity			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	2
Dizziness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	3 / 22 (13.64%)
occurrences (all)	0	0	6
VIth nerve disorder			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Seizure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Pyramidal tract syndrome			

subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	3 / 11 (27.27%)	6 / 9 (66.67%)	8 / 22 (36.36%)
occurrences (all)	11	10	14
Febrile neutropenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Anaemia			
subjects affected / exposed	1 / 11 (9.09%)	3 / 9 (33.33%)	7 / 22 (31.82%)
occurrences (all)	1	4	10
Lymphopenia			
subjects affected / exposed	1 / 11 (9.09%)	6 / 9 (66.67%)	6 / 22 (27.27%)
occurrences (all)	1	10	9
Neutropenia			
subjects affected / exposed	3 / 11 (27.27%)	7 / 9 (77.78%)	9 / 22 (40.91%)
occurrences (all)	15	18	29
Thrombocytopenia			
subjects affected / exposed	0 / 11 (0.00%)	3 / 9 (33.33%)	8 / 22 (36.36%)
occurrences (all)	0	6	12
Eye disorders			
Blindness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Conjunctival hyperaemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Mydriasis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Salivary hypersecretion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Odynophagia			

subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Nausea			
subjects affected / exposed	2 / 11 (18.18%)	1 / 9 (11.11%)	4 / 22 (18.18%)
occurrences (all)	4	1	7
Enteritis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	2 / 22 (9.09%)
occurrences (all)	1	0	2
Dyspepsia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	5 / 22 (22.73%)
occurrences (all)	0	1	9
Constipation			
subjects affected / exposed	2 / 11 (18.18%)	1 / 9 (11.11%)	5 / 22 (22.73%)
occurrences (all)	2	1	5
Abdominal pain			
subjects affected / exposed	3 / 11 (27.27%)	1 / 9 (11.11%)	1 / 22 (4.55%)
occurrences (all)	3	1	6
Stomatitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	2 / 11 (18.18%)	4 / 9 (44.44%)	5 / 22 (22.73%)
occurrences (all)	3	5	6
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 22 (0.00%)
occurrences (all)	0	3	0
Skin and subcutaneous tissue disorders			
Palmar-plantar erythrodysaesthesia syndrome			

subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Eczema			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Dry skin			
subjects affected / exposed	1 / 11 (9.09%)	2 / 9 (22.22%)	0 / 22 (0.00%)
occurrences (all)	1	2	0
Dermatitis acneiform			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	2 / 22 (9.09%)
occurrences (all)	1	0	2
Decubitus ulcer			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Rash maculo-papular			
subjects affected / exposed	0 / 11 (0.00%)	3 / 9 (33.33%)	2 / 22 (9.09%)
occurrences (all)	0	3	2
Rash			
subjects affected / exposed	2 / 11 (18.18%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences (all)	2	0	1
Pruritus			
subjects affected / exposed	2 / 11 (18.18%)	3 / 9 (33.33%)	1 / 22 (4.55%)
occurrences (all)	2	3	1
Urticaria			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Urinary hesitation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0

Urinary retention			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Temporomandibular joint syndrome			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Muscular weakness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Infections and infestations			
Molluscum contagiosum			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Laryngitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Fungal infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Eye infection			

subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Device related infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	3
Otitis externa			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	3	0	0
Parotitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	1 / 11 (9.09%)	1 / 9 (11.11%)	1 / 22 (4.55%)
occurrences (all)	1	1	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 11 (9.09%)	1 / 9 (11.11%)	1 / 22 (4.55%)
occurrences (all)	1	1	1
Rhinovirus infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 11 (0.00%)	3 / 9 (33.33%)	1 / 22 (4.55%)
occurrences (all)	0	3	1
Oral candidiasis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 11 (18.18%)	0 / 9 (0.00%)	3 / 22 (13.64%)
occurrences (all)	3	0	3

Hypercalcaemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Hypernatraemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	1 / 22 (4.55%)
occurrences (all)	0	1	2
Hypoalbuminaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Hypocalcaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	2 / 22 (9.09%)
occurrences (all)	0	1	2
Hypokalaemia			
subjects affected / exposed	2 / 11 (18.18%)	1 / 9 (11.11%)	2 / 22 (9.09%)
occurrences (all)	2	1	2
Hypomagnesaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Hypophosphataemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Medulloblastoma		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 10 (90.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Vascular disorders			

Hypertension			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Flushing			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Pallor			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Gait disturbance			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Asthenia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
General physical health deterioration			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Non-cardiac chest pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Bronchostenosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cough			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Tonsillar inflammation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Sleep apnoea syndrome			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Rhinorrhoea			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hiccups			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypoxia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Pharyngeal erythema			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Respiratory failure			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Personality change			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Confusional state			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		

Anxiety			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Investigations			
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Alanine aminotransferase increased			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	4		
Urine output decreased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Weight increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Upper limb fracture			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Ligament sprain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		

Contusion subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Cardiac disorders Bradycardia subjects affected / exposed occurrences (all) Sinus tachycardia subjects affected / exposed occurrences (all)	 0 / 10 (0.00%) 0 1 / 10 (10.00%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Peripheral sensory neuropathy subjects affected / exposed occurrences (all) Depressed level of consciousness subjects affected / exposed occurrences (all) Ataxia subjects affected / exposed occurrences (all) Aphasia subjects affected / exposed occurrences (all) Hemiparesis subjects affected / exposed occurrences (all) Hydrocephalus subjects affected / exposed occurrences (all) Muscle spasticity subjects affected / exposed occurrences (all) Paraesthesia	 3 / 10 (30.00%) 7 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0		

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
VIth nerve disorder			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Tremor			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Somnolence			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Seizure			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Pyramidal tract syndrome			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	3		
Febrile neutropenia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Anaemia			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Lymphopenia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Neutropenia			
subjects affected / exposed	4 / 10 (40.00%)		
occurrences (all)	7		

Thrombocytopenia			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	3		
Eye disorders			
Blindness			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Conjunctival hyperaemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Mydriasis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Salivary hypersecretion			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Odynophagia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Enteritis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Dysphagia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	3		
Constipation			

subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	3		
Abdominal pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Stomatitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	4 / 10 (40.00%)		
occurrences (all)	5		
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Eczema			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dermatitis acneiform			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Decubitus ulcer			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Rash maculo-papular			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Rash			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Urticaria			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Rash pruritic			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Urinary hesitation			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Urinary retention			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Urinary incontinence			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Temporomandibular joint syndrome			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Muscular weakness			

subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Molluscum contagiosum			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Laryngitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Fungal infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Eye infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Device related infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Bronchitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Otitis externa			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Parotitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		

Pharyngitis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2			
Rhinovirus infection subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Rhinitis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Oral candidiasis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Metabolism and nutrition disorders				
Decreased appetite subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2			
Hypercalcaemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Hypernatraemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Hypoalbuminaemia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1			
Hypocalcaemia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1			
Hypokalaemia				

subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	4		
Hypomagnesaemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		
Hyponatraemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hypophosphataemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 June 2017	Updated exploratory endpoints
18 August 2017	Updated inclusion and exclusion criteria
20 December 2017	Updated exclusion criteria

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported