Clinical trial results:
An Open-Label, Dose-Escalation, Phase I/II Study to Investigate the Safety, Pharmacokinetics, Pharmacodynamics and Clinical Activity of the MEK Inhibitor Trametinib in Children and Adolescents Subjects with Cancer or Plexiform Neurofibromas and Trametinib in Combination with Dabrafenib in Children and Adolescents with Cancers Harboring V600 mutation

Summary

EudraCT number	2013-003596-35
Trial protocol	GB FR
Global end of trial date	29 December 2020

Results information

Result version number	v1 (current)
This version publication date	07 July 2021
First version publication date	07 July 2021

Trial information

Trial identification

Sponsor protocol code	MEK116540

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02124772
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001177-PIP01-11
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	29 December 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 December 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The overall objective of the study was to establish a safe and tolerable dose of trametinib in infants, children, and adolescents and determine preliminary activity of trametinib monotherapy in selected recurrent, refractory or unresectable childhood tumors. In addition, this study also aimed to establish the safety, tolerability and activity of trametinib in combination with dabrafenib in children and adolescents with recurrent, refractory or unresectable BRAF V600 mutated tumors.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 January 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 58
Country: Number of subjects enrolled	Canada: 36
Country: Number of subjects enrolled	France: 23
Country: Number of subjects enrolled	Australia: 7
Country: Number of subjects enrolled	United Kingdom: 15
Worldwide total number of subjects	139
EEA total number of subjects	23

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)	10
Children (2-11 years)	91
Adolescents (12-17 years)	38
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in 16 investigative sites in 5 countries.

Pre-assignment

Screening details:

The participants were screened within 14 days prior to enrollment. After screening, the treatment period started on Cycle 1 Day 1.

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	Part A – TMT 0.0125 mg/kg/day

Arm description:

Participants treated with trametinib 0.0125 mg/kg/day

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

Dosage and administration details:

Trametinib was administered orally, once daily. It was available in tablets (0.125 mg, 0.5 mg, 2 mg dose) as well as in powder form for oral solution (0.05 mg/mL dose).
The administered dose was 0.0125 mg/kg/day

Arm title	Part A – TMT 0.025 mg/kg/day

Arm description:

Participants treated with trametinib 0.025 mg/kg/day

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

Dosage and administration details:

Trametinib was administered orally, once daily. It was available in tablets (0.125 mg, 0.5 mg, 2 mg dose) as well as in powder form for oral solution (0.05 mg/mL dose).
The administered dose was 0.025 mg/kg/day

Arm title	Part A – TMT 0.032 mg/kg/day

Arm description:

Participants under 6 years of age treated with trametinib 0.032 mg/kg/day

Arm type	Experimental

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

Dosage and administration details:

Trametinib was administered orally, once daily. It was available in tablets (0.125 mg, 0.5 mg, 2 mg dose) as well as in powder form for oral solution (0.05 mg/mL dose).
The administered dose was 0.032 mg/kg/day

Arm title	Part A – TMT 0.04 mg/kg/day

Arm description:

Participants treated with trametinib 0.04 mg/kg/day

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

Dosage and administration details:

Trametinib was administered orally, once daily. It was available in tablets (0.125 mg, 0.5 mg, 2 mg dose) as well as in powder form for oral solution (0.05 mg/mL dose).
The administered dose was 0.04 mg/kg/day

Arm title	Part B – Neuroblastoma

Arm description:

Participants with refractory or relapsed neuroblastoma treated with trametinib 0.025 mg/kg/day

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

Dosage and administration details:

Trametinib was administered orally, once daily. It was available in tablets (0.125 mg, 0.5 mg, 2 mg dose) as well as in powder form for oral solution (0.05 mg/mL dose).
The administered dose was 0.025 mg/kg/day

Arm title	Part B – LGG fusion

Arm description:

Participants with refractory or relapsed neuroblastoma treated with trametinib 0.025 mg/kg/day

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

Dosage and administration details:

Trametinib was administered orally, once daily. It was available in tablets (0.125 mg, 0.5 mg, 2 mg dose) as well as in powder form for oral solution (0.05 mg/mL dose).
The administered dose was 0.025 mg/kg/day

Arm title	Part B – NF-1 with PN

Arm description:

Participants with neurofibromatosis Type -1 associated plexiform neurofibromas (NF-1 with PN) treated with trametinib 0.025 mg/kg/day

Arm type	Experimental

Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Oral solution
Routes of administration	Oral use

Dosage and administration details:

Trametinib was administered orally, once daily. It was available in tablets (0.125 mg, 0.5 mg, 2 mg dose) as well as in powder form for oral solution (0.05 mg/mL dose). The administered dose was 0.025 mg/kg/day

Arm title	Part B – BRAF V600 mutant solid tumor

Arm description:

Participants with BRAF V600 mutant solid tumors treated with trametinib 0.025 mg/kg/day

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

Dosage and administration details:

Trametinib was administered orally, once daily. It was available in tablets (0.125 mg, 0.5 mg, 2 mg dose) as well as in powder form for oral solution (0.05 mg/mL dose). The administered dose was 0.025 mg/kg/day

Arm title	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D

Arm description:

Participants treated with a combination therapy of trametinib (0.025 mg/kg/day) plus 50% of the recommended phase II dose (RP2D) of dabrafenib monotherapy (2.63 mg/kg/day for <12 years old subjects and 2.25 mg/kg/day for ≥12 years old subjects)

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

Dosage and administration details:

Trametinib was administered orally, once daily. It was available in tablets (0.125 mg, 0.5 mg, 2 mg dose) as well as in powder form for oral solution (0.05 mg/mL dose). The administered dose was 0.025 mg/kg/day

Investigational medicinal product name	Dabrafenib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Capsule, Oral suspension, Dispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Dabrafenib was administered orally, twice daily. The daily dose was divided into two equal doses. It was available in capsules (50 mg and 75 mg), dispersible tablets (10 mg) and powder for oral suspension (10 mg/mL dose). The administered dose was 50% of the recommended phase II dose (RP2D) of dabrafenib monotherapy: 2.63 mg/kg/day for <12 years old subjects and 2.25 mg/kg/day for ≥12 years old subjects

Arm title	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D

Arm description:

Participants treated with a combination therapy of trametinib (0.025 mg/kg/day) plus 100% of the recommended phase II dose (RP2D) of dabrafenib monotherapy (5.25 mg/kg/day for <12 years old subjects and 4.5 mg/kg/day for ≥12 years old subjects)

Arm type	Experimental

Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Oral solution
Routes of administration	Oral use

Dosage and administration details:

Trametinib was administered orally, once daily. It was available in tablets (0.125 mg, 0.5 mg, 2 mg dose) as well as in powder form for oral solution (0.05 mg/mL dose). The administered dose was 0.025 mg/kg/day

Investigational medicinal product name	Dabrafenib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersible tablet, Capsule, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Dabrafenib was administered orally, twice daily. The daily dose was divided into two equal doses. It was available in capsules (50 mg and 75 mg), dispersible tablets (10 mg) and powder for oral suspension (10 mg/mL dose). The administered dose was 100% of the recommended phase II dose (RP2D) of dabrafenib monotherapy: 5.25 mg/kg/day for <12 years old subjects and 4.5 mg/kg/day for ≥12 years old subjects

Arm title	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D

Arm description:

Participants under 6 years of age treated with a combination therapy of trametinib (0.032 mg/kg/day) with 100% of the recommended phase II dose (RP2D) of dabrafenib monotherapy (5.25 mg/kg/day)

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

Dosage and administration details:

Trametinib was administered orally, once daily. It was available in tablets (0.125 mg, 0.5 mg, 2 mg dose) as well as in powder form for oral solution (0.05 mg/mL dose). The administered dose was 0.032 mg/kg/day

Investigational medicinal product name	Dabrafenib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersible tablet, Capsule, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Dabrafenib was administered orally, twice daily. The daily dose was divided into two equal doses. It was available in capsules (50 mg and 75 mg), dispersible tablets (10 mg) and powder for oral suspension (10 mg/mL dose). The administered dose was 100% of the recommended phase II dose (RP2D) of dabrafenib monotherapy for <12 years old subjects as all participants in this arm were under 6 years of age: 5.25 mg/kg/day.

Arm title	Part D – LGG

Arm description:

Participants with low grade glioma (LGG) treated with a combination therapy of trametinib (0.032 mg/kg/day for < 6 years old subjects and 0.025 mg/kg/day for ≥ 6 years old subjects) plus 100% of the recommended phase II dose (RP2D) of dabrafenib monotherapy (5.25 mg/kg/day for <12 years old subjects and 4.5 mg/kg/day for ≥12 years old subjects)

Arm type	Experimental

Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Oral solution
Routes of administration	Oral use

Dosage and administration details:

Trametinib was administered orally, once daily. It was available in tablets (0.125 mg, 0.5 mg, 2 mg dose) as well as in powder form for oral solution (0.05 mg/mL dose). The administered dose was 0.032 mg/kg/day for < 6 years old subjects and 0.025 mg/kg/day for ≥ 6 years old subjects

Investigational medicinal product name	Dabrafenib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersible tablet, Capsule, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Dabrafenib was administered orally, twice daily. The daily dose was divided into two equal doses. It was available in capsules (50 mg and 75 mg), dispersible tablets (10 mg) and powder for oral suspension (10 mg/mL dose). The administered dose was 100% of the recommended phase II dose (RP2D) of dabrafenib monotherapy: 5.25 mg/kg/day for <12 years old subjects and 4.5 mg/kg/day for ≥12 years old subjects

Arm title	Part D – LCH

Arm description:

Participants with Langerhans cell histiocytosis (LCH) treated with a combination therapy of trametinib (0.032 mg/kg/day for < 6 years old subjects and 0.025 mg/kg/day for ≥ 6 years old subjects) plus 100% of the recommended phase II dose (RP2D) of dabrafenib monotherapy (5.25 mg/kg/day for <12 years old subjects and 4.5 mg/kg/day for ≥12 years old subjects)

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

Dosage and administration details:

Trametinib was administered orally, once daily. It was available in tablets (0.125 mg, 0.5 mg, 2 mg dose) as well as in powder form for oral solution (0.05 mg/mL dose). The administered dose was 0.032 mg/kg/day for < 6 years old subjects and 0.025 mg/kg/day for ≥ 6 years old subjects

Investigational medicinal product name	Dabrafenib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersible tablet, Capsule, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Dabrafenib was administered orally, twice daily. The daily dose was divided into two equal doses. It was available in capsules (50 mg and 75 mg), dispersible tablets (10 mg) and powder for oral suspension (10 mg/mL dose). The administered dose was 100% of the recommended phase II dose (RP2D) of dabrafenib monotherapy: 5.25 mg/kg/day for <12 years old subjects and 4.5 mg/kg/day for ≥12 years old subjects

Number of subjects in period 1	Part A – TMT 0.0125 mg/kg/day	Part A – TMT 0.025 mg/kg/day	Part A – TMT 0.032 mg/kg/day
Started	3	19	12
Completed	0	5	6
Not completed	3	14	6
Adverse event, non-fatal	1	4	1
Withdrawal consent	-	1	1
Not specified	-	7	2
Investigator discretion	-	2	2
Progressive disease	-	-	-
Lack of efficacy	2	-	-

Number of subjects in period 1	Part A – TMT 0.04 mg/kg/day	Part B – Neuroblastoma	Part B – LGG fusion
Started	16	11	10
Completed	3	2	2
Not completed	13	9	8
Adverse event, non-fatal	5	2	1
Withdrawal consent	1	-	1
Not specified	5	4	3
Investigator discretion	1	1	-
Progressive disease	-	-	-
Lack of efficacy	1	2	3

Number of subjects in period 1	Part B – NF-1 with PN	Part B – BRAF V600 mutant solid tumor	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D
Started	10	10	3
Completed	2	1	2
Not completed	8	9	1
Adverse event, non-fatal	1	5	-
Withdrawal consent	1	-	-
Not specified	4	1	1
Investigator discretion	1	-	-
Progressive disease	1	1	-
Lack of efficacy	-	2	-

Number of subjects in period 1	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – LGG
Started	9	6	20
Completed	2	4	14
Not completed	7	2	6
Adverse event, non-fatal	3	1	3
Withdrawal consent	1	-	1
Not specified	1	1	1

Investigator discretion	1	-	1
Progressive disease	-	-	-
Lack of efficacy	1	-	-

Number of subjects in period 1	Part D – LCH
Started	10
Completed	8
Not completed	2
Adverse event, non-fatal	1
Withdrawal consent	-
Not specified	-
Investigator discretion	-
Progressive disease	-
Lack of efficacy	1

Reporting groups	
Reporting group title	Part A – TMT 0.0125 mg/kg/day
Reporting group description:	
Participants treated with trametinib 0.0125 mg/kg/day	
Reporting group title	Part A – TMT 0.025 mg/kg/day
Reporting group description:	
Participants treated with trametinib 0.025 mg/kg/day	
Reporting group title	Part A – TMT 0.032 mg/kg/day
Reporting group description:	
Participants under 6 years of age treated with trametinib 0.032 mg/kg/day	
Reporting group title	Part A – TMT 0.04 mg/kg/day
Reporting group description:	
Participants treated with trametinib 0.04 mg/kg/day	
Reporting group title	Part B – Neuroblastoma
Reporting group description:	
Participants with refractory or relapsed neuroblastoma treated with trametinib 0.025 mg/kg/day	
Reporting group title	Part B – LGG fusion
Reporting group description:	
Participants with refractory or relapsed neuroblastoma treated with trametinib 0.025 mg/kg/day	
Reporting group title	Part B – NF-1 with PN
Reporting group description:	
Participants with neurofibromatosis Type -1 associated plexiform neurofibromas (NF-1 with PN) treated with trametinib 0.025 mg/kg/day	
Reporting group title	Part B – BRAF V600 mutant solid tumor
Reporting group description:	
Participants with BRAF V600 mutant solid tumors treated with trametinib 0.025 mg/kg/day	
Reporting group title	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D
Reporting group description:	
Participants treated with a combination therapy of trametinib (0.025 mg/kg/day) plus 50% of the recommended phase II dose (RP2D) of dabrafenib monotherapy (2.63 mg/kg/day for <12 years old subjects and 2.25 mg/kg/day for ≥12 years old subjects)	
Reporting group title	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D
Reporting group description:	
Participants treated with a combination therapy of trametinib (0.025 mg/kg/day) plus 100% of the recommended phase II dose (RP2D) of dabrafenib monotherapy (5.25 mg/kg/day for <12 years old subjects and 4.5 mg/kg/day for ≥12 years old subjects)	
Reporting group title	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D
Reporting group description:	
Participants under 6 years of age treated with a combination therapy of trametinib (0.032 mg/kg/day) with 100% of the recommended phase II dose (RP2D) of dabrafenib monotherapy (5.25 mg/kg/day)	
Reporting group title	Part D – LGG
Reporting group description:	
Participants with low grade glioma (LGG) treated with a combination therapy of trametinib (0.032 mg/kg/day for < 6 years old subjects and 0.025 mg/kg/day for ≥ 6 years old subjects) plus 100% of the recommended phase II dose (RP2D) of dabrafenib monotherapy (5.25 mg/kg/day for <12 years old subjects and 4.5 mg/kg/day for ≥12 years old subjects)	
Reporting group title	Part D – LCH
Reporting group description:	
Participants with Langerhans cell histiocytosis (LCH) treated with a combination therapy of trametinib (0.032 mg/kg/day for < 6 years old subjects and 0.025 mg/kg/day for ≥ 6 years old subjects) plus 100% of the recommended phase II dose (RP2D) of dabrafenib monotherapy (5.25 mg/kg/day for <12 years old subjects and 4.5 mg/kg/day for ≥12 years old subjects)	

Reporting group values	Part A – TMT 0.0125 mg/kg/day	Part A – TMT 0.025 mg/kg/day	Part A – TMT 0.032 mg/kg/day
Number of subjects	3	19	12
Age Categorical Units: participants			
< 2 years	0	4	1
2 - <6 years	1	5	11
6 - <12 years	1	4	0
≥ 12 years	1	6	0
Age continuous Units: years			
arithmetic mean	9.7	7.2	3.3
standard deviation	± 6.43	± 5.16	± 1.18
Sex: Female, Male Units: participants			
Female	1	7	6
Male	2	12	6
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	1	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	2	0
White	3	16	7
More than one race	0	0	0
Unknown or Not Reported	0	0	5

Reporting group values	Part A – TMT 0.04 mg/kg/day	Part B – Neuroblastoma	Part B – LGG fusion
Number of subjects	16	11	10
Age Categorical Units: participants			
< 2 years	2	1	0
2 - <6 years	0	3	4
6 - <12 years	9	5	5
≥ 12 years	5	2	1
Age continuous Units: years			
arithmetic mean	9.7	8.2	7.0
standard deviation	± 4.99	± 5.18	± 3.56
Sex: Female, Male Units: participants			
Female	7	6	5
Male	9	5	5
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	0	0

Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	2	2
White	14	9	6
More than one race	0	0	0
Unknown or Not Reported	0	0	2

Reporting group values	Part B – NF-1 with PN	Part B – BRAF V600 mutant solid tumor	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D
Number of subjects	10	10	3
Age Categorical Units: participants			
< 2 years	1	0	0
2 - <6 years	4	5	0
6 - <12 years	3	1	1
≥ 12 years	2	4	2
Age continuous Units: years			
arithmetic mean	6.6	7.9	12.7
standard deviation	± 4.86	± 5.20	± 3.06
Sex: Female, Male Units: participants			
Female	5	5	0
Male	5	5	3
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	2	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	0
White	7	5	2
More than one race	1	0	0
Unknown or Not Reported	1	3	0

Reporting group values	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – LGG
Number of subjects	9	6	20
Age Categorical Units: participants			
< 2 years	0	1	0
2 - <6 years	2	5	2
6 - <12 years	2	0	9
≥ 12 years	5	0	9
Age continuous Units: years			
arithmetic mean	10.6	2.7	10.5
standard deviation	± 5.15	± 1.28	± 3.79
Sex: Female, Male Units: participants			
Female	6	4	10
Male	3	2	10

Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	2	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	0
White	6	4	16
More than one race	0	0	0
Unknown or Not Reported	0	2	4

Reporting group values	Part D – LCH	Total	
Number of subjects	10	139	
Age Categorical Units: participants			
< 2 years	0	10	
2 - <6 years	6	48	
6 - <12 years	3	43	
≥ 12 years	1	38	
Age continuous Units: years			
arithmetic mean	5.6		
standard deviation	± 3.63	-	
Sex: Female, Male Units: participants			
Female	2	64	
Male	8	75	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	1	
Asian	1	8	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	9	
White	3	98	
More than one race	1	2	
Unknown or Not Reported	4	21	

End points reporting groups

Reporting group title	Part A – TMT 0.0125 mg/kg/day
Reporting group description:	
Participants treated with trametinib 0.0125 mg/kg/day	
Reporting group title	Part A – TMT 0.025 mg/kg/day
Reporting group description:	
Participants treated with trametinib 0.025 mg/kg/day	
Reporting group title	Part A – TMT 0.032 mg/kg/day
Reporting group description:	
Participants under 6 years of age treated with trametinib 0.032 mg/kg/day	
Reporting group title	Part A – TMT 0.04 mg/kg/day
Reporting group description:	
Participants treated with trametinib 0.04 mg/kg/day	
Reporting group title	Part B – Neuroblastoma
Reporting group description:	
Participants with refractory or relapsed neuroblastoma treated with trametinib 0.025 mg/kg/day	
Reporting group title	Part B – LGG fusion
Reporting group description:	
Participants with refractory or relapsed neuroblastoma treated with trametinib 0.025 mg/kg/day	
Reporting group title	Part B – NF-1 with PN
Reporting group description:	
Participants with neurofibromatosis Type -1 associated plexiform neurofibromas (NF-1 with PN) treated with trametinib 0.025 mg/kg/day	
Reporting group title	Part B – BRAF V600 mutant solid tumor
Reporting group description:	
Participants with BRAF V600 mutant solid tumors treated with trametinib 0.025 mg/kg/day	
Reporting group title	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D
Reporting group description:	
Participants treated with a combination therapy of trametinib (0.025 mg/kg/day) plus 50% of the recommended phase II dose (RP2D) of dabrafenib monotherapy (2.63 mg/kg/day for <12 years old subjects and 2.25 mg/kg/day for ≥12 years old subjects)	
Reporting group title	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D
Reporting group description:	
Participants treated with a combination therapy of trametinib (0.025 mg/kg/day) plus 100% of the recommended phase II dose (RP2D) of dabrafenib monotherapy (5.25 mg/kg/day for <12 years old subjects and 4.5 mg/kg/day for ≥12 years old subjects)	
Reporting group title	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D
Reporting group description:	
Participants under 6 years of age treated with a combination therapy of trametinib (0.032 mg/kg/day) with 100% of the recommended phase II dose (RP2D) of dabrafenib monotherapy (5.25 mg/kg/day)	
Reporting group title	Part D – LGG
Reporting group description:	
Participants with low grade glioma (LGG) treated with a combination therapy of trametinib (0.032 mg/kg/day for < 6 years old subjects and 0.025 mg/kg/day for ≥ 6 years old subjects) plus 100% of the recommended phase II dose (RP2D) of dabrafenib monotherapy (5.25 mg/kg/day for <12 years old subjects and 4.5 mg/kg/day for ≥12 years old subjects)	
Reporting group title	Part D – LCH
Reporting group description:	
Participants with Langerhans cell histiocytosis (LCH) treated with a combination therapy of trametinib (0.032 mg/kg/day for < 6 years old subjects and 0.025 mg/kg/day for ≥ 6 years old subjects) plus 100% of the recommended phase II dose (RP2D) of dabrafenib monotherapy (5.25 mg/kg/day for <12 years old subjects and 4.5 mg/kg/day for ≥12 years old subjects)	

Subject analysis set title	Part B – All tumor types TMT 0.025 mg/kg/day
Subject analysis set type	Full analysis

Subject analysis set description:

Participants (all tumor types in Part B) treated with trametinib 0.025 mg/kg/day

Subject analysis set title	Part D – All tumor types TMT 0.032 mg/kg/day + 100% DRB RP2D
Subject analysis set type	Full analysis

Subject analysis set description:

Participants under 6 years of age (all tumor types in Part D) treated with a combination therapy of trametinib (0.032 mg/kg/day) with 100% of the recommended phase II dose (RP2D) of dabrafenib monotherapy (5.25 mg/kg/day)

Subject analysis set title	Part D – All tumor types TMT 0.025 mg/kg/day + 100% DRB RP2D
Subject analysis set type	Full analysis

Subject analysis set description:

Participants (all tumor types in Part D) treated with a combination therapy of trametinib (0.025 mg/kg/day) plus 100% of the recommended phase II dose (RP2D) of dabrafenib monotherapy (5.25 mg/kg/day for <12 years old subjects and 4.5 mg/kg/day for ≥12 years old subjects)

Subject analysis set title	Part A, B, C and D – All participants with PK data
Subject analysis set type	Full analysis

Subject analysis set description:

Participants in the study (all doses and all tumor types) with available pharmacokinetic data

Subject analysis set title	Part D – All tumor types TMT 0.032 mg/kg/day + 100% DRB RP2D
Subject analysis set type	Full analysis

Subject analysis set description:

Participants under 6 years of age (all tumor types in Part D) treated with a combination therapy of trametinib (0.032 mg/kg/day) with 100% of the recommended phase II dose (RP2D) of dabrafenib monotherapy (5.25 mg/kg/day)

Subject analysis set title	TMT 0.0125 mg/kg/day
Subject analysis set type	Full analysis

Subject analysis set description:

Participants treated with trametinib oral solution at a dose level of 0.0125 mg/kg/day

Subject analysis set title	TMT 0.025 mg/kg/day
Subject analysis set type	Full analysis

Subject analysis set description:

Participants treated with trametinib oral solution at a dose level of 0.025 mg/kg/day

Subject analysis set title	TMT 0.032 mg/kg/day
Subject analysis set type	Full analysis

Subject analysis set description:

Participants treated with trametinib oral solution at a dose level of 0.032 mg/kg/day

Subject analysis set title	TMT 0.04 mg/kg/day
Subject analysis set type	Full analysis

Subject analysis set description:

Participants treated with trametinib oral solution at a dose level of 0.04 mg/kg/day

Subject analysis set title	TMT 0.025 mg/kg/day + 50% DRB RP2D
Subject analysis set type	Full analysis

Subject analysis set description:

Participants treated with a combination therapy of trametinib (0.025 mg/kg/day) plus 50% of the RP2D of dabrafenib monotherapy (oral suspension formulation)

Subject analysis set title	TMT 0.025 mg/kg/day + 100% DRB RP2D
Subject analysis set type	Full analysis

Subject analysis set description:

Participants treated with a combination therapy of trametinib (0.025 mg/kg/day) plus 100% of the RP2D of dabrafenib monotherapy (oral suspension formulation)

Subject analysis set title	TMT 0.032 mg/kg/day + 100% DRB RP2D
Subject analysis set type	Full analysis

Subject analysis set description:

Participants treated with a combination therapy of trametinib (0.032 mg/kg/day) plus 100% of the RP2D of dabrafenib monotherapy (oral suspension formulation)

Primary: Incidence of treatment emergent adverse events in subjects treated with trametinib monotherapy

End point title	Incidence of treatment emergent adverse events in subjects treated with trametinib monotherapy[1][2]

End point description:

Incidence of treatment emergent adverse events is defined as number of participants with adverse events (AEs) and serious adverse events (SAEs), including changes from baseline in vital signs and laboratory results qualifying and reported as AEs. The number of participants in each category is reported in the table.

End point type	Primary

End point timeframe:

From the day of the first dose of trametinib up to 30 days after the last dose, up to maximum duration of 64 months

Notes:

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

[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 only applies to subjects treated with trametinib monotherapy.

End point values	Part A – TMT 0.0125 mg/kg/day	Part A – TMT 0.025 mg/kg/day	Part A – TMT 0.032 mg/kg/day	Part A – TMT 0.04 mg/kg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	19	12	16
Units: participants				
AEs	3	19	12	16
Treatment-related AEs	3	19	12	16
SAEs	1	8	3	11
Treatment-related SAEs	0	5	1	6
Fatal SAEs	0	0	0	0
AEs leading to discontinuation	1	4	1	6
AEs requiring dose interruptions	0	12	6	14
AEs requiring dose reductions	0	9	5	9
AEs requiring dose reductions or interruptions	0	13	7	14

End point values	Part B – Neuroblastoma	Part B – LGG fusion	Part B – NF-1 with PN	Part B – BRAF V600 mutant solid tumor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	10	10	10
Units: participants				
AEs	11	10	10	10
Treatment-related AEs	10	10	10	10
SAEs	6	6	6	5

Treatment-related SAEs	1	2	2	3
Fatal SAEs	0	0	0	0
AEs leading to discontinuation	4	1	1	5
AEs requiring dose interruptions	3	8	5	8
AEs requiring dose reductions	2	4	3	7
AEs requiring dose reductions or interruptions	3	8	6	9

Statistical analyses

No statistical analyses for this end point

Primary: Average steady state plasma concentration (Cavg) of trametinib when administered alone (monotherapy)

End point title	Average steady state plasma concentration (Cavg) of trametinib when administered alone (monotherapy)[3][4]

End point description:

Pharmacokinetic (PK) parameters were calculated based on trametinib plasma concentrations by using non-compartmental methods. The average steady state plasma concentration (Cavg) of trametinib was calculated as the ratio of area under the curve (AUC)/tau, where tau = 24 h for trametinib.

End point type	Primary

End point timeframe:

pre dose, 1, 2, 4, 7, 10 and 24 hours post trametinib dose on Cycle 1 Day 15. The duration of 1 cycle was 28 days.

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: No statistical analysis were planned for this primary endpoint.

[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 only applies to subjects treated with trametinib monotherapy.

End point values	Part A – TMT 0.0125 mg/kg/day	Part A – TMT 0.025 mg/kg/day	Part A – TMT 0.032 mg/kg/day	Part A – TMT 0.04 mg/kg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	18	9	15
Units: ng/mL				
geometric mean (geometric coefficient of variation)	5.76 (± 24.8)	13.9 (± 27.1)	15.2 (± 16.9)	21.3 (± 20.7)

End point values	Part B – Neuroblastoma	Part B – LGG fusion	Part B – NF-1 with PN	Part B – BRAF V600 mutant solid tumor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	10	9
Units: ng/mL				
geometric mean (geometric coefficient of variation)	15.1 (± 36.0)	13.2 (± 40.4)	13.5 (± 25.1)	15.8 (± 42.8)

End point values	Part B – All tumor types TMT 0.025 mg/kg/day			
Subject group type	Subject analysis set			
Number of subjects analysed	38			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	14.3 (± 35.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Trough concentration (Ctrough) of trametinib when administered alone and in combination with dabrafenib

End point title	Trough concentration (Ctrough) of trametinib when administered alone and in combination with dabrafenib

End point description:

Pharmacokinetic (PK) parameters were calculated based on trametinib plasma concentrations by using non-compartmental methods. Ctrough is defined as the observed plasma concentration just prior to the beginning of, or at the end, of a dosing interval.
Due to EudraCT system limitations, data fields cannot be blank if the number of subjects analyzed in the corresponding column is greater than 0. Therefore, not applicable values (coefficient of variation when n=1) are indicated as '999'.

End point type	Secondary

End point timeframe:

pre dose on Cycle 1 Day 15. The duration of 1 cycle was 28 days.

End point values	Part A – TMT 0.0125 mg/kg/day	Part A – TMT 0.025 mg/kg/day	Part A – TMT 0.032 mg/kg/day	Part A – TMT 0.04 mg/kg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	19	9	15
Units: ng/mL				
geometric mean (geometric coefficient of variation)	4.37 (± 30.6)	11.1 (± 44.0)	10.2 (± 19.4)	15.6 (± 30.1)

End point values	Part B – Neuroblastoma	Part B – LGG fusion	Part B – NF-1 with PN	Part B – BRAF V600 mutant solid tumor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	10	9
Units: ng/mL				
geometric mean (geometric coefficient	10.7 (± 43.3)	9.45 (± 53.6)	9.25 (± 29.0)	11.3 (± 50.3)

of variation)

End point values	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – LGG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	1	6	20
Units: ng/mL				
geometric mean (geometric coefficient of variation)	8.31 (± 999)	10.2 (± 999)	3.86 (± 34.9)	8.60 (± 42.2)

End point values	Part D – LCH	Part B – All tumor types TMT 0.025 mg/kg/day	Part D – All tumor types TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – All tumor types TMT 0.025 mg/kg/day + 100% DRB RP2D
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	38	5	21
Units: ng/mL				
geometric mean (geometric coefficient of variation)	3.74 (± 66.3)	10.1 (± 43.6)	3.05 (± 50.7)	8.68 (± 38.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum observed plasma concentration (Cmax) of trametinib when administered alone and in combination with dabrafenib

End point title	Maximum observed plasma concentration (Cmax) of trametinib when administered alone and in combination with dabrafenib

End point description:

Pharmacokinetic (PK) parameters were calculated based on trametinib plasma concentrations by using non-compartmental methods. Cmax is defined as the maximum (peak) observed plasma concentration following a dose.
Due to EudraCT system limitations, data fields cannot be blank if the number of subjects analyzed in the corresponding column is greater than 0. Therefore, not applicable values (coefficient of variation when n=1) are indicated as '999'.

End point type	Secondary

End point timeframe:

pre dose, 1, 2, 4, 7, 10 and 24 hours post trametinib dose on Cycle 1 Day 15 (part A and B) and pre dose, 0.5, 1, 2, 3, 4, 6 and 8 hours post trametinib dose on Cycle 1 Day 15 (part C and D). The duration of 1 cycle was 28 days.

End point values	Part A – TMT 0.0125 mg/kg/day	Part A – TMT 0.025 mg/kg/day	Part A – TMT 0.032 mg/kg/day	Part A – TMT 0.04 mg/kg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	18	9	16
Units: ng/mL				
geometric mean (geometric coefficient of variation)	9.61 (± 32.9)	21.1 (± 33.3)	26.1 (± 16.8)	32.6 (± 28.9)

End point values	Part B – Neuroblastoma	Part B – LGG fusion	Part B – NF-1 with PN	Part B – BRAF V600 mutant solid tumor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	10	9
Units: ng/mL				
geometric mean (geometric coefficient of variation)	26.6 (± 39.6)	22.1 (± 41.9)	21.6 (± 26.1)	27.5 (± 31.6)

End point values	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – LGG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	1	6	20
Units: ng/mL				
geometric mean (geometric coefficient of variation)	26.0 (± 999)	24.5 (± 999)	23.7 (± 36.3)	22.9 (± 29.2)

End point values	Part D – LCH	Part B – All tumor types TMT 0.025 mg/kg/day	Part D – All tumor types TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – All tumor types TMT 0.025 mg/kg/day + 100% DRB RP2D
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	38	5	21
Units: ng/mL				
geometric mean (geometric coefficient of variation)	15.6 (± 52.5)	24.2 (± 35.6)	25.9 (± 35.8)	20.0 (± 38.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to reach maximum plasma concentration (Tmax) of trametinib when administered alone and in combination with dabrafenib

End point title	Time to reach maximum plasma concentration (Tmax) of trametinib when administered alone and in combination with dabrafenib

End point description:

Pharmacokinetic (PK) parameters were calculated based on trametinib plasma concentrations by using non-compartmental methods. Tmax is defined as the time to reach maximum (peak) plasma concentration following a dose.

End point type	Secondary

End point timeframe:

pre dose, 1, 2, 4, 7, 10 and 24 hours post trametinib dose on Cycle 1 Day 15 (part A and B) and pre dose, 0.5, 1, 2, 3, 4, 6 and 8 hours post trametinib dose on Cycle 1 Day 15 (part C and D). The duration of 1 cycle was 28 days.

End point values	Part A – TMT 0.0125 mg/kg/day	Part A – TMT 0.025 mg/kg/day	Part A – TMT 0.032 mg/kg/day	Part A – TMT 0.04 mg/kg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	19	9	16
Units: hours				
median (full range (min-max))	1.00 (1.00 to 2.00)	2.00 (1.00 to 4.00)	1.00 (1.00 to 2.00)	2.00 (1.00 to 24.0)

End point values	Part B – Neuroblastoma	Part B – LGG fusion	Part B – NF-1 with PN	Part B – BRAF V600 mutant solid tumor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	10	9
Units: hours				
median (full range (min-max))	1.00 (1.00 to 4.00)	1.50 (1.00 to 2.00)	1.00 (1.00 to 2.00)	1.00 (1.00 to 2.00)

End point values	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – LGG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	1	6	20
Units: hours				
median (full range (min-max))	1.00 (1.00 to 1.00)	1.00 (1.00 to 1.00)	1.50 (1.00 to 2.00)	2.00 (1.00 to 3.00)

End point values	Part D – LCH	Part B – All tumor types TMT 0.025 mg/kg/day	Part D – All tumor types TMT 0.032 mg/kg/day + 100% DRB	Part D – All tumor types TMT 0.025 mg/kg/day + 100% DRB

			RP2D	RP2D
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	38	5	21
Units: hours				
median (full range (min-max))	1.00 (1.00 to 4.00)	1.00 (1.00 to 4.00)	1.00 (1.00 to 1.00)	2.00 (1.00 to 4.00)

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma concentration-time curve from time zero to the time of last quantifiable concentration (AUClast) of trametinib when administered alone and in combination with dabrafenib

End point title	Area under the plasma concentration-time curve from time zero to the time of last quantifiable concentration (AUClast) of trametinib when administered alone and in combination with dabrafenib

End point description:

Pharmacokinetic (PK) parameters were calculated based on trametinib plasma concentrations by using non-compartmental methods. The linear trapezoidal method was used for area under the curve calculation.
Due to EudraCT system limitations, data fields cannot be blank if the number of subjects analyzed in the corresponding column is greater than 0. Therefore, not applicable values (coefficient of variation when n=1) are indicated as '999'.

End point type	Secondary

End point timeframe:

pre dose, 1, 2, 4, 7, 10 and 24 hours post trametinib dose on Cycle 1 Day 15 (part A and B) and pre dose, 0.5, 1, 2, 3, 4, 6 and 8 hours post trametinib dose on Cycle 1 Day 15 (part C and D). The duration of 1 cycle was 28 days.

End point values	Part A – TMT 0.0125 mg/kg/day	Part A – TMT 0.025 mg/kg/day	Part A – TMT 0.032 mg/kg/day	Part A – TMT 0.04 mg/kg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	19	9	16
Units: hours*ng/mL				
geometric mean (geometric coefficient of variation)	138 (± 24.8)	341 (± 28.3)	364 (± 16.9)	413 (± 76.2)

End point values	Part B – Neuroblastoma	Part B – LGG fusion	Part B – NF-1 with PN	Part B – BRAF V600 mutant solid tumor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	10	9
Units: hours*ng/mL				
geometric mean (geometric coefficient of variation)	362 (± 36.0)	316 (± 40.4)	304 (± 36.9)	379 (± 42.8)

End point values	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – LGG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	1	6	20
Units: hours*ng/mL				
geometric mean (geometric coefficient of variation)	290 (± 999)	331 (± 999)	122 (± 29.0)	270 (± 35.8)

End point values	Part D – LCH	Part B – All tumor types TMT 0.025 mg/kg/day	Part D – All tumor types TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – All tumor types TMT 0.025 mg/kg/day + 100% DRB RP2D
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	38	5	21
Units: hours*ng/mL				
geometric mean (geometric coefficient of variation)	118 (± 53.4)	337 (± 38.6)	126 (± 30.7)	255 (± 49.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma concentration-time curve from time zero to the end of the dosing interval tau at steady-state (AUCtau) of trametinib when administered alone and in combination with dabrafenib

End point title	Area under the plasma concentration-time curve from time zero to the end of the dosing interval tau at steady-state (AUCtau) of trametinib when administered alone and in combination with dabrafenib

End point description:

Pharmacokinetic (PK) parameters were calculated based on trametinib plasma concentrations by using non-compartmental methods. The linear trapezoidal method was used for area under the curve calculation. The duration of the dosing interval (tau) was 24 hours for trametinib.
Due to EudraCT system limitations, data fields cannot be blank if the number of subjects analyzed in the corresponding column is greater than 0. Therefore, not applicable values (coefficient of variation when n=1) are indicated as '999'.

End point type	Secondary

End point timeframe:

pre dose, 1, 2, 4, 7, 10 and 24 hours post trametinib dose on Cycle 1 Day 15 (part A and B) and pre dose, 0.5, 1, 2, 3, 4, 6 and 8 hours post trametinib dose on Cycle 1 Day 15 (part C and D). The duration of 1 cycle was 28 days.

End point values	Part A – TMT 0.0125 mg/kg/day	Part A – TMT 0.025 mg/kg/day	Part A – TMT 0.032 mg/kg/day	Part A – TMT 0.04 mg/kg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	18	9	15
Units: hours*ng/mL				
geometric mean (geometric coefficient of variation)	138 (± 24.8)	334 (± 27.1)	364 (± 16.9)	511 (± 20.7)

End point values	Part B – Neuroblastoma	Part B – LGG fusion	Part B – NF-1 with PN	Part B – BRAF V600 mutant solid tumor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	10	9
Units: hours*ng/mL				
geometric mean (geometric coefficient of variation)	362 (± 36.0)	316 (± 40.4)	323 (± 25.1)	379 (± 42.8)

End point values	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – LGG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	1	6	20
Units: hours*ng/mL				
geometric mean (geometric coefficient of variation)	290 (± 999)	331 (± 999)	236 (± 28.4)	308 (± 20.0)

End point values	Part D – LCH	Part B – All tumor types TMT 0.025 mg/kg/day	Part D – All tumor types TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – All tumor types TMT 0.025 mg/kg/day + 100% DRB RP2D
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	38	5	21
Units: hours*ng/mL				
geometric mean (geometric coefficient of variation)	186 (± 23.7)	343 (± 35.8)	228 (± 33.1)	286 (± 28.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent plasma clearance (CL/F) of trametinib when administered alone and in combination with dabrafenib

End point title	Apparent plasma clearance (CL/F) of trametinib when administered alone and in combination with dabrafenib

End point description:

Pharmacokinetic (PK) parameters were calculated based on trametinib plasma concentrations by using non-compartmental methods. Apparent plasma clearance (CL/F) values were calculated as Dose/AUCtau.
Due to EudraCT system limitations, data fields cannot be blank if the number of subjects analyzed in the corresponding column is greater than 0. Therefore, not applicable values (coefficient of variation when n=1) are indicated as '999'.

End point type	Secondary

End point timeframe:

pre dose, 1, 2, 4, 7, 10 and 24 hours post trametinib dose on Cycle 1 Day 15 (part A and B) and pre dose, 0.5, 1, 2, 3, 4, 6 and 8 hours post trametinib dose on Cycle 1 Day 15 (part C and D). The duration of 1 cycle was 28 days.

End point values	Part A – TMT 0.0125 mg/kg/day	Part A – TMT 0.025 mg/kg/day	Part A – TMT 0.032 mg/kg/day	Part A – TMT 0.04 mg/kg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	18	9	15
Units: mL/hour				
geometric mean (geometric coefficient of variation)	2750 (± 69.4)	1530 (± 64.5)	1240 (± 25.5)	2040 (± 71.5)

End point values	Part B – Neuroblastoma	Part B – LGG fusion	Part B – NF-1 with PN	Part B – BRAF V600 mutant solid tumor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	10	9
Units: mL/hour				
geometric mean (geometric coefficient of variation)	1710 (± 55.6)	1910 (± 47.8)	1590 (± 65.3)	1820 (± 42.6)

End point values	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – LGG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	1	6	20
Units: mL/hour				
geometric mean (geometric coefficient of variation)	2590 (± 999)	3770 (± 999)	2010 (± 38.5)	3540 (± 54.0)

End point values	Part D – LCH	Part B – All tumor types TMT 0.025	Part D – All tumor types TMT 0.032	Part D – All tumor types TMT 0.025

		mg/kg/day	mg/kg/day + 100% DRB RP2D	mg/kg/day + 100% DRB RP2D
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	38	5	21
Units: mL/hour				
geometric mean (geometric coefficient of variation)	3060 (± 44.9)	1750 (± 51.5)	2180 (± 23.9)	3810 (± 49.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Average steady state plasma concentration (Cavg) of trametinib when administered in combination with dabrafenib

End point title	Average steady state plasma concentration (Cavg) of trametinib when administered in combination with dabrafenib[5]

End point description:

Pharmacokinetic (PK) parameters were calculated based on trametinib plasma concentrations by using non-compartmental methods. The average steady state plasma concentration (Cavg) of trametinib was calculated as the ratio of area under the curve (AUC)/tau, where tau = 24 h for trametinib.
Due to EudraCT system limitations, data fields cannot be blank if the number of subjects analyzed in the corresponding column is greater than 0. Therefore, not applicable values (coefficient of variation when n=1) are indicated as '999'.

End point type	Secondary

End point timeframe:

pre dose, 0.5, 1, 2, 3, 4, 6 and 8 hours post trametinib dose on Cycle 1 Day 15. The duration of 1 cycle was 28 days.

Notes:

[5] - 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 only applies to subjects treated with trametinib in combination with dabrafenib.

End point values	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – LGG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	1	6	20
Units: ng/mL				
geometric mean (geometric coefficient of variation)	12.1 (± 999)	13.8 (± 999)	9.83 (± 28.4)	12.8 (± 20.0)

End point values	Part D – LCH	Part D – All tumor types TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – All tumor types TMT 0.025 mg/kg/day + 100% DRB RP2D	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	5	21	

Units: ng/mL				
geometric mean (geometric coefficient of variation)	7.76 (± 23.7)	9.50 (± 33.1)	11.9 (± 28.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of treatment emergent adverse events in subjects treated with trametinib in combination with dabrafenib

End point title	Incidence of treatment emergent adverse events in subjects treated with trametinib in combination with dabrafenib[6]

End point description:

Incidence of treatment emergent adverse events is defined as number of participants with adverse events (AEs) and serious adverse events (SAEs), including changes from baseline in vital signs and laboratory results qualifying and reported as AEs. The number of participants in each category is reported in the table.

End point type	Secondary

End point timeframe:

From the day of the first dose of the combination up to 30 days after the last dose, up to maximum duration of 53 months

Notes:

[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 only applies to subjects treated with trametinib in combination with dabrafenib.

End point values	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – LGG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	9	6	20
Units: participants				
AEs	3	9	6	20
Treatment-related AEs	3	9	6	20
SAEs	1	5	2	8
Treatment-related SAEs	0	2	1	5
Fatal SAEs	0	0	0	0
AEs leading to discontinuation	0	3	1	5
AEs requiring dose interruptions	1	6	4	16
AEs requiring dose reductions	1	3	1	6
AEs requiring dose reductions or interruptions	1	7	4	16

End point values	Part D – LCH			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: participants				

AEs	10			
Treatment-related AEs	10			
SAEs	6			
Treatment-related SAEs	3			
Fatal SAEs	0			
AEs leading to discontinuation	1			
AEs requiring dose interruptions	8			
AEs requiring dose reductions	1			
AEs requiring dose reductions or interruptions	8			

Statistical analyses

No statistical analyses for this end point

Secondary: Best Overall Response (BOR) based on RECIST v1.1, RANO and Dombi criteria and as per investigator assessment

End point title	Best Overall Response (BOR) based on RECIST v1.1, RANO and Dombi criteria and as per investigator assessment

End point description:

Response evaluations were assessed using Response Evaluation Criteria in Solid Tumors v1.1 (RECIST v1.1) for subjects with solid tumors except neuroblastomas, primary central nervous system tumors (gliomas) or plexiform neurofibromas (PNs).
Response evaluations for subjects with neuroblastomas could have included: measureable disease (by CT/MRI alone) assessed according to RECIST v1.1, evaluable disease assessed for meta-iodobenzylguanidine (MIBG) response, and biochemical (urine HVA/VMA) with bone marrow involvement assessed by Hematoxylin and Eosin staining of bilateral bone marrow biopsies and aspirates.
Response evaluations for glioma subjects was assessed using Response Assessment in Neuro Oncology (RANO) criteria with solid tumors through MRI scans.
Response evaluations of PNs were assessed using volumetric determination and Dombi criteria through MRI scans.
The number of participants in each response category is reported in the table.

End point type	Secondary

End point timeframe:

From the day of the first dose of any study drug up to the last dose, up to maximum duration of 63 months

End point values	Part A – TMT 0.0125 mg/kg/day	Part A – TMT 0.025 mg/kg/day	Part A – TMT 0.032 mg/kg/day	Part A – TMT 0.04 mg/kg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	19	12	16
Units: participants				
Complete response (CR)	0	0	0	0
Partial response (PR)	0	1	1	0
Stable disease (SD)	1	2	3	4
Progressive disease (PD)	0	0	2	0
Non-CR/Non-PD	0	0	0	0
Unknown	0	0	0	2
Missing	2	16	6	10

End point values	Part B – Neuroblastoma	Part B – LGG fusion	Part B – NF-1 with PN	Part B – BRAF V600 mutant solid tumor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	10	10	10
Units: participants				
Complete response (CR)	0	0	0	0
Partial response (PR)	1	3	0	5
Stable disease (SD)	1	7	8	4
Progressive disease (PD)	5	0	0	1
Non-CR/Non-PD	0	0	0	0
Unknown	1	0	0	0
Missing	3	0	2	0

End point values	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – LGG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	9	6	20
Units: participants				
Complete response (CR)	0	0	2	2
Partial response (PR)	2	3	2	9
Stable disease (SD)	1	5	1	8
Progressive disease (PD)	0	1	0	0
Non-CR/Non-PD	0	0	0	0
Unknown	0	0	0	1
Missing	0	0	1	0

End point values	Part D – LCH			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: participants				
Complete response (CR)	3			
Partial response (PR)	3			
Stable disease (SD)	3			
Progressive disease (PD)	0			
Non-CR/Non-PD	0			
Unknown	0			
Missing	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response rate (ORR) based on RECIST v1.1, RANO and Dombi criteria and as per investigator assessment

End point title	Objective response rate (ORR) based on RECIST v1.1, RANO and Dombi criteria and as per investigator assessment

End point description:

Objective response rate (ORR) was defined as the percentage of subjects with best overall response rate (BOR) with confirmation of complete response (CR) or partial response (PR) according to criteria for a specific disease type, among subjects with disease assessment at baseline. BOR for each subject was determined from the sequence of overall responses according to the rules for RECIST v1.1, RANO and Dombi criteria. ORR was calculated based on the investigator assessment of tumor response data and was based on confirmed responses.

End point type	Secondary

End point timeframe:

From the day of the first dose of any study drug up to the last dose, up to maximum duration of 63 months

End point values	Part A – TMT 0.0125 mg/kg/day	Part A – TMT 0.025 mg/kg/day	Part A – TMT 0.032 mg/kg/day	Part A – TMT 0.04 mg/kg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	19	12	16
Units: percentage of participants				
number (confidence interval 95%)	0 (0.0 to 70.8)	5.3 (0.1 to 26.0)	8.3 (0.2 to 38.5)	0 (0.0 to 20.6)

End point values	Part B – Neuroblastoma	Part B – LGG fusion	Part B – NF-1 with PN	Part B – BRAF V600 mutant solid tumor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	10	10	10
Units: percentage of participants				
number (confidence interval 95%)	9.1 (0.2 to 41.3)	30.0 (6.7 to 65.2)	0 (0.0 to 30.8)	50.0 (18.7 to 81.3)

End point values	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – LGG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	9	6	20
Units: percentage of participants				
number (confidence interval 95%)	66.7 (9.4 to 99.2)	33.3 (7.5 to 70.1)	66.7 (22.3 to 95.7)	55.0 (31.5 to 76.9)

End point values	Part D – LCH			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
number (confidence interval 95%)	60.0 (26.2 to 87.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Rate (CBR) based on RECIST v1.1, RANO and Dombi criteria and as per investigator assessment

End point title	Clinical Benefit Rate (CBR) based on RECIST v1.1, RANO and Dombi criteria and as per investigator assessment

End point description:

Clinical Benefit Rate (CBR) was defined as the percentage of subjects with best overall response rate (BOR) with confirmation of complete response (CR), partial response (PR) or stable disease (SD) according to criteria for a specific disease type, among subjects with disease assessment at baseline. BOR for each subject was determined from the sequence of overall responses according to the rules for RECIST v1.1, RANO and Dombi criteria. ORR was calculated based on the investigator assessment of tumor response data and was based on confirmed responses.

End point type	Secondary

End point timeframe:

From the day of the first dose of any study drug up to the last dose, up to maximum duration of 63 months

End point values	Part A – TMT 0.0125 mg/kg/day	Part A – TMT 0.025 mg/kg/day	Part A – TMT 0.032 mg/kg/day	Part A – TMT 0.04 mg/kg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	19	12	16
Units: percentage of participants				
number (confidence interval 95%)	33.3 (0.8 to 90.6)	15.8 (3.4 to 39.6)	33.3 (9.9 to 65.1)	25.0 (7.3 to 52.4)

End point values	Part B – Neuroblastoma	Part B – LGG fusion	Part B – NF-1 with PN	Part B – BRAF V600 mutant solid tumor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	10	10	10
Units: percentage of participants				
number (confidence interval 95%)	18.2 (2.3 to 51.8)	100 (69.2 to 100)	80.0 (44.4 to 97.5)	90.0 (55.5 to 99.7)

End point values	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – LGG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	9	6	20
Units: percentage of participants				
number (confidence interval 95%)	100 (29.2 to 100)	88.9 (51.8 to 99.7)	83.3 (35.9 to 99.6)	95.0 (75.1 to 99.9)

End point values	Part D – LCH			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
number (confidence interval 95%)	90.0 (55.5 to 99.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent clearance (CL/F) of trametinib estimated with a PopPK model

End point title	Apparent clearance (CL/F) of trametinib estimated with a PopPK model

End point description:

The population pharmacokinetic (PopPK) model of trametinib can be described using a two-compartment model with dual sequential 1st order absorption (Ka1, Ka2) and 1st order elimination. Apparent clearance (CL/F) of trametinib estimated with the PopPK model is summarized in this record.

End point type	Secondary

End point timeframe:

pre dose, 1, 2, 4, 7, 10 and 24 hours post trametinib dose on Cycle 1 Day 15 (part A and B) and pre dose, 0.5, 1, 2, 3, 4, 6 and 8 hours post trametinib dose on Cycle 1 Day 15 (part C and D). The duration of 1 cycle was 28 days.

End point values	Part A, B, C and D – All participants with PK data			
Subject group type	Subject analysis set			
Number of subjects analysed	133			
Units: liters/hour				
number (not applicable)	5.07			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent central volume (Vc/F) of trametinib estimated with a PopPK model

End point title	Apparent central volume (Vc/F) of trametinib estimated with a PopPK model

End point description:

The population pharmacokinetic (PopPK) model of trametinib can be described using a two-compartment model with dual sequential 1st order absorption (Ka1, Ka2) and 1st order elimination. Apparent central volume (Vc/F) of trametinib estimated with the PopPK model is summarized in this record.

End point type	Secondary

End point timeframe:

pre dose, 1, 2, 4, 7, 10 and 24 hours post trametinib dose on Cycle 1 Day 15 (part A and B) and pre dose, 0.5, 1, 2, 3, 4, 6 and 8 hours post trametinib dose on Cycle 1 Day 15 (part C and D). The duration of 1 cycle was 28 days.

End point values	Part A, B, C and D – All participants with PK data			
Subject group type	Subject analysis set			
Number of subjects analysed	133			
Units: liters	184			

Statistical analyses

No statistical analyses for this end point

Secondary: Absorption rate constants (Ka1 and Ka2) of trametinib estimated with a PopPK model

End point title	Absorption rate constants (Ka1 and Ka2) of trametinib estimated with a PopPK model

End point description:

The population pharmacokinetic (PopPK) model of trametinib can be described using a two-compartment model with dual sequential 1st order absorption (Ka1, Ka2) and 1st order elimination. The absorption rate constants (Ka1 and Ka2) estimated with the PopPK model are summarized in this record.

End point type	Secondary

End point timeframe:

pre dose, 1, 2, 4, 7, 10 and 24 hours post trametinib dose on Cycle 1 Day 15 (part A and B) and pre dose, 0.5, 1, 2, 3, 4, 6 and 8 hours post trametinib dose on Cycle 1 Day 15 (part C and D). The duration of 1 cycle was 28 days.

End point values	Part A, B, C and D – All participants with PK data			
Subject group type	Subject analysis set			
Number of subjects analysed	133			
Units: 1/hours				
number (not applicable)				
Ka1	0.134			
Ka2	1.55			

Statistical analyses

No statistical analyses for this end point

Secondary: Significant covariates estimated with a PopPK model

End point title	Significant covariates estimated with a PopPK model

End point description:

The population pharmacokinetic (PopPK) model of trametinib can be described using a two-compartment model with dual sequential 1st order absorption (Ka1, Ka2) and 1st order elimination. Sex and weight are significant covariates on apparent clearance (CL/F), and weight is also a significant covariate on apparent intercompartmental clearance (Q/F). Use of dabrafenib, yes or no, is a covariate on the relative bioavailability of trametinib, reflecting the effect of dabrafenib on the PK of trametinib.
The estimates of these covariates (effect of weight on CL/F, effect of sex on CL/F, effect of weight on Q/F, effect of combination with dabrafenib on relative bioavailability F1) calculated with the PopPK model are summarized in this record.

End point type	Secondary

End point timeframe:

pre dose, 1, 2, 4, 7, 10 and 24 hours post trametinib dose on Cycle 1 Day 15 (part A and B) and pre dose, 0.5, 1, 2, 3, 4, 6 and 8 hours post trametinib dose on Cycle 1 Day 15 (part C and D). The duration of 1 cycle was 28 days.

End point values	Part A, B, C and D – All participants with PK data			
Subject group type	Subject analysis set			
Number of subjects analysed	133			
Units: no units				
number (not applicable)				
Effect of weight on CL/F	0.788			
Effect of sex on CL/F	1.24			
Effect of weight on Q/F	0.679			
Effect of combination with dabrafenib on F1	0.876			

Statistical analyses

No statistical analyses for this end point

Secondary: Trough concentration (Ctrough) of dabrafenib when administered in combination with trametinib

End point title	Trough concentration (Ctrough) of dabrafenib when administered in combination with trametinib[7]

End point description:

Pharmacokinetic (PK) parameters were calculated based on dabrafenib plasma concentrations by using non-compartmental methods. Ctrough is defined as the observed plasma concentration just prior to the beginning of, or at the end, of a dosing interval.

End point type	Secondary

End point timeframe:

pre dose on Cycle 1 Day 15. The duration of 1 cycle was 28 days.

Notes:

[7] - 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 only applies to subjects treated with trametinib in combination with dabrafenib.

End point values	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – LGG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	7	6	19
Units: ng/mL				
geometric mean (geometric coefficient of variation)	88.9 (± 99.6)	28.6 (± 203.5)	8.10 (± 159.6)	38.2 (± 130.9)

End point values	Part D – LCH	Part D – All tumor types TMT 0.025 mg/kg/day + 100% DRB RP2D	Part D – All tumor types TMT 0.032 mg/kg/day + 100% DRB RP2D	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	21	6	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	11.8 (± 869.4)	42.7 (± 137.4)	5.36 (± 429.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum observed plasma concentration (Cmax) of dabrafenib when administered in combination with trametinib

End point title	Maximum observed plasma concentration (Cmax) of dabrafenib when administered in combination with trametinib[8]

End point description:

Pharmacokinetic (PK) parameters were calculated based on dabrafenib plasma concentrations by using non-compartmental methods. Cmax is defined as the maximum (peak) observed plasma concentration following a dose.

End point type	Secondary

End point timeframe:

pre dose, 0.5, 1, 2, 3, 4, 6 and 8 hours post dabrafenib dose on Cycle 1 Day 15. The duration of 1 cycle was 28 days.

Notes:

[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 only applies to subjects treated with trametinib in combination with dabrafenib.

End point values	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – LGG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	7	6	19
Units: ng/mL				
geometric mean (geometric coefficient of variation)	630 (± 235.2)	1560 (± 35.3)	1440 (± 43.3)	1360 (± 55.6)

End point values	Part D – LCH	Part D – All tumor types TMT 0.025 mg/kg/day + 100% DRB RP2D	Part D – All tumor types TMT 0.032 mg/kg/day + 100% DRB RP2D	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	21	6	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	1490 (± 88.1)	1290 (± 68.7)	1840 (± 35.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to reach maximum plasma concentration (Tmax) of dabrafenib when administered in combination with trametinib

End point title	Time to reach maximum plasma concentration (Tmax) of dabrafenib when administered in combination with trametinib[9]

End point description:

Pharmacokinetic (PK) parameters were calculated based on dabrafenib plasma concentrations by using non-compartmental methods. Tmax is defined as the time to reach maximum (peak) plasma concentration following a dose.

End point type	Secondary

End point timeframe:

pre dose, 0.5, 1, 2, 3, 4, 6 and 8 hours post dabrafenib dose on Cycle 1 Day 15. The duration of 1 cycle was 28 days.

Notes:

[9] - 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 only applies to subjects treated with trametinib in combination with dabrafenib.

End point values	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – LGG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	7	6	19
Units: hours				
median (full range (min-max))	2.00 (2.00 to 4.00)	1.00 (1.00 to 2.00)	2.00 (1.00 to 2.00)	2.00 (1.00 to 3.00)

End point values	Part D – LCH	Part D – All tumor types TMT 0.025 mg/kg/day + 100% DRB RP2D	Part D – All tumor types TMT 0.032 mg/kg/day + 100% DRB RP2D	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	21	6	
Units: hours				
median (full range (min-max))	1.00 (1.00 to 3.00)	2.00 (1.00 to 3.00)	1.00 (1.00 to 3.00)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma concentration-time curve from time zero to the time of last quantifiable concentration (AUClast) of dabrafenib when administered in combination with trametinib

End point title	Area under the plasma concentration-time curve from time zero to the time of last quantifiable concentration (AUClast) of dabrafenib when administered in combination with trametinib[10]

End point description:

Pharmacokinetic (PK) parameters were calculated based on dabrafenib plasma concentrations by using non-compartmental methods. The linear trapezoidal method was used for area under the curve calculation.

End point type	Secondary

End point timeframe:

pre dose, 0.5, 1, 2, 3, 4, 6 and 8 hours post dabrafenib dose on Cycle 1 Day 15. The duration of 1 cycle was 28 days.

Notes:

[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 only applies to subjects treated with trametinib in combination with dabrafenib.

End point values	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – LGG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	7	6	19
Units: hours*ng/mL				
geometric mean (geometric coefficient of variation)	2560 (± 157.1)	4160 (± 24.6)	3910 (± 48.8)	4030 (± 46.4)

End point values	Part D – LCH	Part D – All tumor types TMT 0.025 mg/kg/day + 100% DRB RP2D	Part D – All tumor types TMT 0.032 mg/kg/day + 100% DRB RP2D	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	21	6	
Units: hours*ng/mL				
geometric mean (geometric coefficient of variation)	3800 (± 35.4)	3950 (± 46.9)	3990 (± 28.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma concentration-time curve from time zero to the end of the dosing interval tau at steady-state (AUCtau) of dabrafenib when administered in combination with trametinib

End point title	Area under the plasma concentration-time curve from time zero to the end of the dosing interval tau at steady-state (AUCtau) of dabrafenib when administered in combination with trametinib[11]

End point description:

Pharmacokinetic (PK) parameters were calculated based on dabrafenib plasma concentrations by using non-compartmental methods. The linear trapezoidal method was used for area under the curve calculation. The duration of the dosing interval (tau) was 12 hours for dabrafenib.

End point type	Secondary

End point timeframe:

pre dose, 0.5, 1, 2, 3, 4, 6 and 8 hours post dabrafenib dose on Cycle 1 Day 15. The duration of 1 cycle was 28 days.

Notes:

[11] - 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 only applies to subjects treated with trametinib in combination with dabrafenib.

End point values	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – LGG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	7	6	19
Units: hours*ng/mL				
geometric mean (geometric coefficient of variation)	2870 (± 116.6)	4160 (± 24.6)	4040 (± 47.9)	4070 (± 46.7)

End point values	Part D – LCH	Part D – All tumor types TMT 0.025 mg/kg/day + 100% DRB RP2D	Part D – All tumor types TMT 0.032 mg/kg/day + 100% DRB RP2D	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	21	6	
Units: hours*ng/mL				
geometric mean (geometric coefficient of variation)	3910 (± 37.4)	3990 (± 47.3)	4150 (± 30.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent plasma clearance (CL/F) of dabrafenib when administered in combination with trametinib

End point title	Apparent plasma clearance (CL/F) of dabrafenib when administered in combination with trametinib[12]

End point description:

Pharmacokinetic (PK) parameters were calculated based on dabrafenib plasma concentrations by using non-compartmental methods. Apparent plasma clearance (CL/F) values were calculated as Dose/AUCtau.

End point type	Secondary

End point timeframe:

pre dose, 0.5, 1, 2, 3, 4, 6 and 8 hours post dabrafenib dose on Cycle 1 Day 15. The duration of 1 cycle was 28 days.

Notes:

[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 only applies to subjects treated with trametinib in combination with dabrafenib.

End point values	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – LGG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	7	6	19
Units: mL/hour				
geometric mean (geometric coefficient of variation)	22900 (± 191.2)	20400 (± 45.4)	10100 (± 67.0)	25400 (± 70.5)

End point values	Part D – LCH	Part D – All tumor types TMT 0.025 mg/kg/day + 100% DRB RP2D	Part D – All tumor types TMT 0.032 mg/kg/day + 100% DRB RP2D	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	21	6	
Units: mL/hour				
geometric mean (geometric coefficient of variation)	12500 (± 63.0)	25100 (± 69.3)	10200 (± 41.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Average steady state plasma concentration (Cavg) of dabrafenib when administered in combination with trametinib

End point title	Average steady state plasma concentration (Cavg) of dabrafenib when administered in combination with trametinib[13]

End point description:

Pharmacokinetic (PK) parameters were calculated based on dabrafenib plasma concentrations by using non-compartmental methods. The average steady state plasma concentration (Cavg) of dabrafenib was calculated as the ratio of area under the curve (AUC)/tau, where tau = 12 h for dabrafenib.

End point type	Secondary

End point timeframe:

pre dose, 0.5, 1, 2, 3, 4, 6 and 8 hours post dabrafenib dose on Cycle 1 Day 15. The duration of 1 cycle was 28 days.

Notes:

[13] - 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 only applies to subjects treated with trametinib in combination with dabrafenib.

End point values	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – LGG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	7	6	19
Units: ng/mL				
geometric mean (geometric coefficient of variation)	239 (± 116.6)	347 (± 24.6)	337 (± 47.9)	339 (± 46.7)

End point values	Part D – LCH	Part D – All tumor types TMT 0.025 mg/kg/day + 100% DRB RP2D	Part D – All tumor types TMT 0.032 mg/kg/day + 100% DRB RP2D	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	21	6	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	326 (± 37.4)	332 (± 47.3)	346 (± 30.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Palatability of trametinib oral solution in pediatric subjects assessed by palatability questionnaire

End point title	Palatability of trametinib oral solution in pediatric subjects assessed by palatability questionnaire

End point description:

For subjects ≥ 12 years of age who received the trametinib oral solution, the subject completed a form to evaluate the various properties of the solution (e.g., bitterness, sweetness, appearance, texture and overall taste). For subjects < 12 years of age who received the solution, their caregiver (e.g. parent or guardian) evaluated the solution with the child based on verbal and non-verbal feedback. The questionnaire was completed after the first dose of study drug and no later than Day 8 (±3 days). Subjects completed a form for each drug separately if enrolled in Parts C and D.

End point type	Secondary

End point timeframe:

After the first dose of trametinib oral solution and no later than Day 8 (±3 days)

End point values	TMT 0.0125 mg/kg/day	TMT 0.025 mg/kg/day	TMT 0.032 mg/kg/day	TMT 0.04 mg/kg/day
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	29	21	4
Units: participants				
Was the medicine difficult to mix?|Yes	0	1	1	0
Was the medicine difficult to mix?|No	2	26	19	4

Was the medicine difficult to mix?|Missing	0	2	1	0
Was the medicine difficult to measure?|Yes	0	0	2	0
Was the medicine difficult to measure?|No	2	29	18	4
Was the medicine difficult to measure?|Missing	0	0	1	0
Was the medicine difficult to administer?|Yes	0	5	5	1
Was the medicine difficult to administer?|No	2	24	15	3
Was the medicine difficult to administer?|Missing	0	0	1	0
Did the subject like the taste?|Yes	2	8	6	2
Did the subject like the taste?|No	0	16	13	1
Did the subject like the taste?|Missing	0	5	2	1
Did subject have difficulty in taking it?|Yes	0	6	7	1
Did subject have difficulty in taking it?|No	2	19	13	3
Did subject have difficulty in taking it?|Missing	0	4	1	0
Did subject resist taking the medicine?|Yes	0	7	6	1
Did subject resist taking the medicine?|No	2	18	14	3
Did subject resist taking the medicine?|Missing	0	4	1	0
Was the medicine bitter?|Yes	0	3	0	0
Was the medicine bitter?|No	0	2	1	0
Was the medicine bitter?|Missing	2	24	20	4
Was the medicine sweet?|Yes	0	2	1	0
Was the medicine sweet?|No	0	3	0	0
Was the medicine sweet?|Missing	2	24	20	4
Was the medicine sour?|Yes	0	2	0	0
Was the medicine sour?|No	0	3	1	0
Was the medicine sour?|Missing	2	24	20	4
Was the medicine gritty?|Yes	0	1	0	0
Was the medicine gritty?|No	0	4	1	0
Was the medicine gritty?|Missing	2	24	20	4
Was the medicine difficult to swallow?|Yes	0	1	0	0
Was the medicine difficult to swallow?|No	0	5	1	0
Was the medicine difficult to swallow?|Missing	2	23	20	4

Statistical analyses

No statistical analyses for this end point

Secondary: Palatability of dabrafenib oral suspension in pediatric subjects assessed by palatability questionnaire

End point title	Palatability of dabrafenib oral suspension in pediatric subjects

	assessed by palatability questionnaire

End point description:

For subjects ≥ 12 years of age who received the dabrafenib suspension, the subject completed a form to evaluate the various properties of the suspension (e.g., bitterness, sweetness, appearance, texture and overall taste). For subjects < 12 years of age who received the suspension, their caregiver (e.g. parent or guardian) evaluated the suspension with the child based on verbal and non-verbal feedback. The questionnaire was completed after the first dose of study drug and no later than Day 8 (±3 days). Subjects completed a form for each drug separately if enrolled in Parts C and D.

End point type	Secondary

End point timeframe:

After the first dose of dabrafenib oral suspension and no later than Day 8 (±3 days)

End point values	TMT 0.025 mg/kg/day + 50% DRB RP2D	TMT 0.025 mg/kg/day + 100% DRB RP2D	TMT 0.032 mg/kg/day + 100% DRB RP2D	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[14]	4	6	
Units: participants				
Was the medicine difficult to mix?|Yes		0	1	
Was the medicine difficult to mix?|No		4	5	
Was the medicine difficult to mix?|Missing		0	0	
Was the medicine difficult to measure?|Yes		0	1	
Was the medicine difficult to measure?|No		4	5	
Was the medicine difficult to measure?|Missing		0	0	
Was the medicine difficult to administer?|Yes		0	1	
Was the medicine difficult to administer?|No		4	5	
Was the medicine difficult to administer?|Missing		0	0	
Did the subject like the taste?|Yes		0	4	
Did the subject like the taste?|No		1	2	
Did the subject like the taste?|Missing		3	0	
Did subject have difficulty in taking it?|Yes		0	2	
Did subject have difficulty in taking it?|No		1	4	
Did subject have difficulty in taking it?|Missing		3	0	
Did subject resist taking the medicine?|Yes		0	4	
Did subject resist taking the medicine?|No		1	2	
Did subject resist taking the medicine?|Missing		3	0	
Was the medicine bitter?|Yes		1	0	
Was the medicine bitter?|No		2	0	
Was the medicine bitter?|Missing		1	6	
Was the medicine sweet?|Yes		0	0	
Was the medicine sweet?|No		3	0	

Was the medicine sweet?|Missing		1	6	
Was the medicine sour?|Yes		2	0	
Was the medicine sour?|No		1	0	
Was the medicine sour?|Missing		1	6	
Was the medicine gritty?|Yes		1	0	
Was the medicine gritty?|No		2	0	
Was the medicine gritty?|Missing		1	6	
Was the medicine difficult to swallow?|Yes		0	0	
Was the medicine difficult to swallow?|No		3	0	
Was the medicine difficult to swallow?|Missing		1	6	

Notes:

[14] - 0 participants filled in the palatability form

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

From the day of the first dose of any study drug up to 30 days after the last dose, up to maximum duration of 64 months.

Adverse event reporting additional description:

Any sign or symptom that occurs during the study treatment plus the 30 days post treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Part A – TMT 0.0125 mg/kg/day

Reporting group description:

Participants treated with trametinib 0.0125 mg/kg/day

Reporting group title	Part A – TMT 0.025 mg/kg/day

Reporting group description:

Participants treated with trametinib 0.025 mg/kg/day

Reporting group title	Part A – TMT 0.032 mg/kg/day

Reporting group description:

Participants under 6 years of age treated with trametinib 0.032 mg/kg/day

Reporting group title	Part A – TMT 0.04 mg/kg/day

Reporting group description:

Participants treated with trametinib 0.04 mg/kg/day

Reporting group title	Part B – Neuroblastoma

Reporting group description:

Participants with refractory or relapsed neuroblastoma treated with trametinib 0.025 mg/kg/day

Reporting group title	Part B – LGG fusion

Reporting group description:

Participants with recurrent or unresectable low grade glioma (LGG) with BRAF tandem duplication with fusion treated with trametinib 0.025 mg/kg/day

Reporting group title	Part B – NF-1 with PN

Reporting group description:

Participants with neurofibromatosis Type -1 associated plexiform neurofibromas (NF-1 with PN) treated with trametinib 0.025 mg/kg/day

Reporting group title	Part B – BRAF V600 mutant solid tumor

Reporting group description:

Participants with BRAF V600 mutant solid tumors treated with trametinib 0.025 mg/kg/day

Reporting group title	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D

Reporting group description:

Participants treated with a combination therapy of trametinib (0.025 mg/kg/day) plus 50% of the recommended phase II dose (RP2D) of dabrafenib monotherapy (2.63 mg/kg/day for <12 years old subjects and 2.25 mg/kg/day for ≥12 years old subjects)

Reporting group title	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D

Reporting group description:

Participants treated with a combination therapy of trametinib (0.025 mg/kg/day) plus 100% of the recommended phase II dose (RP2D) of dabrafenib monotherapy (5.25 mg/kg/day for <12 years old subjects and 4.5 mg/kg/day for ≥12 years old subjects)

Reporting group title	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D

Reporting group description:

Participants under 6 years of age treated with a combination therapy of trametinib (0.032 mg/kg/day)

with 100% of the recommended phase II dose (RP2D) of dabrafenib monotherapy (5.25 mg/kg/day)

Reporting group title	Part D – LGG

Reporting group description:

Participants with low grade glioma (LGG) treated with a combination therapy of trametinib (0.032 mg/kg/day for < 6 years old subjects and 0.025 mg/kg/day for ≥ 6 years old subjects) plus 100% of the recommended phase II dose (RP2D) of dabrafenib monotherapy (5.25 mg/kg/day for <12 years old subjects and 4.5 mg/kg/day for ≥12 years old subjects)

Reporting group title	Part D – LCH

Reporting group description:

Participants with Langerhans cell histiocytosis (LCH) treated with a combination therapy of trametinib (0.032 mg/kg/day for < 6 years old subjects and 0.025 mg/kg/day for ≥ 6 years old subjects) plus 100% of the recommended phase II dose (RP2D) of dabrafenib monotherapy (5.25 mg/kg/day for <12 years old subjects and 4.5 mg/kg/day for ≥12 years old subjects)

Serious adverse events	Part A – TMT 0.0125 mg/kg/day	Part A – TMT 0.025 mg/kg/day	Part A – TMT 0.032 mg/kg/day
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	8 / 19 (42.11%)	3 / 12 (25.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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			
Gastrointestinal tube insertion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Hypothermia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Influenza like illness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Mucosal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (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
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	1 / 4	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (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
Lung disorder			

subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Tonsillar hypertrophy			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (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
Psychiatric disorders			
Restlessness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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 alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (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

Blood bilirubin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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 culture positive			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (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
C-reactive protein increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Ejection fraction decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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			
Accidental overdose			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Femur fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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

Foot fracture			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (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
Hip fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Upper limb fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Vascular access complication			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Wound secretion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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			
Bradycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Tachycardia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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

Balance disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Brain oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Depressed level of consciousness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Dysarthria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Encephalopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Epilepsy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Hydrocephalus			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial pressure increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Pyramidal tract syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Syncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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			
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Anal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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

Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Pancreatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (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
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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			
Adrenal insufficiency			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Kyphosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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 in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Spinal instability			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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			
Adenovirus infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Arthritis infective			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Bronchiolitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (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
Cellulitis			

subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Enterobacter infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Enterococcal bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (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
Escherichia infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	0 / 12 (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
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Lymphangitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Medical device site infection			

subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (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
Osteomyelitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (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
Paronychia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Parotitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Pelvic abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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 streptococcal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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 / 3 (0.00%)	2 / 19 (10.53%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			

subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (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
Rotavirus infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (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 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Skin infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (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
Tonsillitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (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
Varicella			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Vascular device infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Viral infection			

subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (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
Hypernatraemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (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

Serious adverse events	Part A – TMT 0.04 mg/kg/day	Part B – Neuroblastoma	Part B – LGG fusion
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 16 (68.75%)	6 / 11 (54.55%)	6 / 10 (60.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Gastrointestinal tube insertion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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			
Fatigue			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (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
Hypothermia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza like illness			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (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
Mucosal inflammation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (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
Oedema peripheral			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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	1 / 16 (6.25%)	2 / 11 (18.18%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (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
Cough			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (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
Lung disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Tonsillar hypertrophy			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Psychiatric disorders			
Restlessness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (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
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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 bilirubin increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (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
Blood culture positive			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
C-reactive protein increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Ejection fraction decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Weight decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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

White blood cell count decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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			
Accidental overdose			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Femur fracture			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (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
Foot fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Hip fracture			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (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
Upper limb fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Vascular access complication			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound secretion			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (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

Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (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
Tachycardia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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			
Ataxia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (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
Balance disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Brain oedema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Depressed level of consciousness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Dysarthria			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Encephalopathy			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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

Epilepsy			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (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
Headache			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Intracranial pressure increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Pyramidal tract syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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	3 / 16 (18.75%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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			

Neutropenia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Pancreatitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (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
Vomiting			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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			
Haematuria			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Kyphosis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (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
Muscular weakness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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 in extremity			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal instability			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (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
Infections and infestations			
Adenovirus infection			

subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Arthritis infective			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Cellulitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (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
Device related infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterobacter infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (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
Enterococcal bacteraemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Escherichia infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (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
Gastroenteritis			

subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Influenza			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Lymphangitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medical device site infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Paronychia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Parotitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Pelvic abscess			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (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
Pharyngitis			

subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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 streptococcal			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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 / 16 (0.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Rotavirus infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Skin infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (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
Tonsillitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Upper respiratory tract infection			

subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Varicella			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (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
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (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
Dehydration			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (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
Hypernatraemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			

subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (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

Serious adverse events	Part B – NF-1 with PN	Part B – BRAF V600 mutant solid tumor	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 10 (60.00%)	5 / 10 (50.00%)	1 / 3 (33.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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 / 10 (0.00%)	0 / 10 (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			
Gastrointestinal tube insertion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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			
Fatigue			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Hypothermia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Influenza like illness			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Mucosal inflammation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Oedema peripheral			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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	2 / 10 (20.00%)	2 / 10 (20.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (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
Cough			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	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
Hypoxia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Lung disorder			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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 / 10 (0.00%)	1 / 10 (10.00%)	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
Respiratory distress			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Tonsillar hypertrophy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Psychiatric disorders			
Restlessness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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 alkaline phosphatase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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 bilirubin increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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 culture positive			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
C-reactive protein increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Ejection fraction decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Weight decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
White blood cell count decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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			
Accidental overdose			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (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
Femur fracture			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Foot fracture			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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

Hip fracture			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Upper limb fracture			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Vascular access complication			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Wound secretion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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			
Bradycardia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Tachycardia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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			
Ataxia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Balance disorder			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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

Brain oedema			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Depressed level of consciousness			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	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
Dysarthria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Encephalopathy			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (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
Epilepsy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Headache			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Hydrocephalus			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (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
Intracranial pressure increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	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
Posterior reversible encephalopathy syndrome			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Pyramidal tract syndrome			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	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
Seizure			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	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
Syncope			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (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
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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 / 10 (0.00%)	0 / 10 (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
Anal haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Diarrhoea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Nausea			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Pancreatitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Vomiting			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	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
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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			
Haematuria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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			
Adrenal insufficiency			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Kyphosis			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Muscular weakness			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	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
Pain in extremity			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Spinal instability			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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			
Adenovirus infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Arthritis infective			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Bronchiolitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Cellulitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Device related infection			

subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterobacter infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Enterococcal bacteraemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Escherichia infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Gastroenteritis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	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
Influenza			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	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
Lymphangitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Medical device site infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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 / 10 (0.00%)	0 / 10 (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
Paronychia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (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
Parotitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Pelvic abscess			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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 / 10 (0.00%)	1 / 10 (10.00%)	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
Pharyngitis streptococcal			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Pneumonia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Pyelonephritis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Rotavirus infection			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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 / 10 (0.00%)	1 / 10 (10.00%)	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
Skin infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Tonsillitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Upper respiratory tract infection			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 3 (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
Varicella			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (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
Vascular device infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Viral infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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			
Decreased appetite			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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
Dehydration			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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 / 10 (0.00%)	0 / 10 (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
Hypernatraemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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 / 10 (0.00%)	1 / 10 (10.00%)	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

Serious adverse events	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – LGG
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 9 (55.56%)	2 / 6 (33.33%)	8 / 20 (40.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Surgical and medical procedures			
Gastrointestinal tube insertion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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			
Fatigue			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Hypothermia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Influenza like illness			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Mucosal inflammation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Oedema peripheral			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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	3 / 9 (33.33%)	1 / 6 (16.67%)	4 / 20 (20.00%)
occurrences causally related to treatment / all	1 / 3	0 / 4	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Aspiration			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Cough			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 20 (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
Hypoxia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Lung disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillar hypertrophy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Psychiatric disorders			
Restlessness			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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 alkaline phosphatase increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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 bilirubin increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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 culture positive			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
C-reactive protein increased			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (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
Ejection fraction decreased			
subjects affected / exposed	2 / 9 (22.22%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	4 / 4	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Femur fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Foot fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Hip fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Upper limb fracture			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (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
Vascular access complication			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Wound secretion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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			

Bradycardia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Tachycardia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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			
Ataxia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (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
Balance disorder			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (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
Brain oedema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Depressed level of consciousness			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Dysarthria			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (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
Encephalopathy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Epilepsy			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Headache			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Hydrocephalus			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Intracranial pressure increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyramidal tract syndrome			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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			
Neutropenia			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Anal haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Diarrhoea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Nausea			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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	2 / 9 (22.22%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	4 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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			

Haematuria			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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			
Adrenal insufficiency			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kyphosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Muscular weakness			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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 in extremity			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Spinal instability			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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			
Adenovirus infection			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Arthritis infective			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Bronchiolitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Cellulitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Device related infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Enterobacter infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Enterococcal bacteraemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Escherichia infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Gastroenteritis			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Influenza			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Lymphangitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Medical device site infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Paronychia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Parotitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Pelvic abscess			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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 streptococcal			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Pyelonephritis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Rotavirus infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Skin infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Tonsillitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			

subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 20 (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
Varicella			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 20 (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
Vascular device infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Viral infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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			
Decreased appetite			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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
Dehydration			
subjects affected / exposed	1 / 9 (11.11%)	1 / 6 (16.67%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	1 / 4	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypernatraemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (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	Part D – LCH		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 10 (60.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Gastrointestinal tube insertion			
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			
Fatigue			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypothermia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Influenza like illness			

subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mucosal inflammation				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oedema peripheral				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	4 / 10 (40.00%)			
occurrences causally related to treatment / all	7 / 12			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Aspiration				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cough				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung disorder				
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			
Respiratory distress				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tonsillar hypertrophy				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Restlessness				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine aminotransferase increased				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Aspartate aminotransferase increased				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Blood alkaline phosphatase increased				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood bilirubin increased				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Blood culture positive				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
C-reactive protein increased				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ejection fraction decreased				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Weight decreased				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
White blood cell count decreased				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Accidental overdose				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Femur fracture				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Foot fracture				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Hip fracture				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper limb fracture				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular access complication				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound secretion				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Bradycardia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tachycardia				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Ataxia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Balance disorder				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Brain oedema				
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			
Dysarthria				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Encephalopathy				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
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			
Hydrocephalus				
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			
Posterior reversible encephalopathy syndrome				

subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyramidal tract syndrome				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
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			
Gastrointestinal disorders				
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			
Anal haemorrhage				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Kyphosis			

subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain in extremity				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal instability				
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				
Adenovirus infection				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arthritis infective				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchiolitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device related infection				

subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterobacter infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterococcal bacteraemia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lymphangitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Medical device site infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				

subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Paronychia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Parotitis				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Pelvic abscess				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pharyngitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pharyngitis streptococcal				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	0 / 1			
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			
Pyelonephritis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rotavirus 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			
Skin infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tonsillitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Varicella				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular device infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Viral infection				
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				
Decreased appetite				

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypernatraemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Part A – TMT 0.0125 mg/kg/day	Part A – TMT 0.025 mg/kg/day	Part A – TMT 0.032 mg/kg/day
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	19 / 19 (100.00%)	12 / 12 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Neoplasm progression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Skin papilloma			

subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Tumour pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	3 / 12 (25.00%)
occurrences (all)	0	4	3
Lymphoedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pallor			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Surgical and medical procedures			
Central venous catheter removal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tonsillectomy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	4 / 19 (21.05%)	0 / 12 (0.00%)
occurrences (all)	0	4	0
Catheter site hypersensitivity			

subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Catheter site pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Catheter site rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Chills			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	1 / 12 (8.33%)
occurrences (all)	0	2	1
Cyst			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	1 / 12 (8.33%)
occurrences (all)	0	2	1
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)	10 / 19 (52.63%)	9 / 12 (75.00%)
occurrences (all)	1	14	11
Feeling cold			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Gait disturbance			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Granuloma			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Hypothermia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	2 / 12 (16.67%)
occurrences (all)	0	1	4
Localised oedema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	4 / 19 (21.05%)	1 / 12 (8.33%)
occurrences (all)	0	8	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	4 / 19 (21.05%)	0 / 12 (0.00%)
occurrences (all)	0	9	0
Pain			
subjects affected / exposed	0 / 3 (0.00%)	3 / 19 (15.79%)	1 / 12 (8.33%)
occurrences (all)	0	5	1
Peripheral swelling			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	1 / 12 (8.33%)
occurrences (all)	0	2	1
Pyrexia			
subjects affected / exposed	1 / 3 (33.33%)	11 / 19 (57.89%)	8 / 12 (66.67%)
occurrences (all)	2	33	18
Swelling face			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Xerosis			

subjects affected / exposed	0 / 3 (0.00%)	4 / 19 (21.05%)	2 / 12 (16.67%)
occurrences (all)	0	6	2
Immune system disorders			
Allergy to arthropod sting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Perineal rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Vulvovaginal pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Apnoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Aspiration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	1 / 3 (33.33%)	7 / 19 (36.84%)	6 / 12 (50.00%)
occurrences (all)	1	18	12
Dysphonia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Dyspnoea exertional			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	1 / 3 (33.33%)	9 / 19 (47.37%)	4 / 12 (33.33%)
occurrences (all)	1	9	5
Hypoxia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Laryngeal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	1 / 12 (8.33%)
occurrences (all)	0	2	1
Nasal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nasal odour			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	4 / 19 (21.05%)	1 / 12 (8.33%)
occurrences (all)	0	9	3
Pharyngeal swelling			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Productive cough			

subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Respiratory disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Respiratory tract congestion			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Rhinitis allergic			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Rhinorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	4 / 12 (33.33%)
occurrences (all)	0	2	9
Sinus congestion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Sneezing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Snoring			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tachypnoea			
subjects affected / exposed	0 / 3 (0.00%)	3 / 19 (15.79%)	1 / 12 (8.33%)
occurrences (all)	0	8	1
Throat irritation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tonsillar hypertrophy			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Wheezing			

subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Agitation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	1 / 12 (8.33%)
occurrences (all)	0	2	1
Attention deficit hyperactivity disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Delirium			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	2
Dyssomnia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Enuresis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Initial insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Insomnia			

subjects affected / exposed	0 / 3 (0.00%)	4 / 19 (21.05%)	1 / 12 (8.33%)
occurrences (all)	0	4	1
Irritability			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	1 / 12 (8.33%)
occurrences (all)	0	2	1
Mood altered			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Obsessive-compulsive disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Restlessness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	3 / 19 (15.79%)	1 / 12 (8.33%)
occurrences (all)	0	3	1
Albumin urine present			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Anion gap decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 3 (33.33%)	8 / 19 (42.11%)	4 / 12 (33.33%)
occurrences (all)	1	9	7
Bacterial test positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	4
Blood albumin decreased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	5 / 19 (26.32%)	0 / 12 (0.00%)
occurrences (all)	0	8	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Blood bicarbonate increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood chloride increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	3 / 19 (15.79%)	1 / 12 (8.33%)
occurrences (all)	0	3	1
Blood glucose increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood urea decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Body temperature fluctuation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ejection fraction decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1

Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram ST-T segment abnormal			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram T wave amplitude decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
End-tidal CO2 decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Grip strength decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Haematocrit increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Haemoglobin decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Haemoglobin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Lung diffusion test decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	2 / 12 (16.67%)
occurrences (all)	0	2	3
Lymphocyte count increased			

subjects affected / exposed	0 / 3 (0.00%)	3 / 19 (15.79%)	0 / 12 (0.00%)
occurrences (all)	0	3	0
Lymphocyte percentage decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Neutrophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Neutrophil percentage increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Nitrite urine present			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Protein total decreased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 19 (5.26%)	2 / 12 (16.67%)
occurrences (all)	1	1	2
Protein urine			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Red blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Red blood cells urine			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Red blood cells urine positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Specific gravity urine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Staphylococcus test positive			

subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Urine ketone body present			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Urine leukocyte esterase positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	3
Urine output decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	1 / 12 (8.33%)
occurrences (all)	0	2	1
Weight increased			
subjects affected / exposed	0 / 3 (0.00%)	5 / 19 (26.32%)	3 / 12 (25.00%)
occurrences (all)	0	8	3
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	3 / 12 (25.00%)
occurrences (all)	0	2	7
White blood cell count increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
White blood cells urine positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	3
pH urine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Contusion			

subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Fracture			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Gastrostomy tube site complication			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Hand fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Head injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Incision site pruritus			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Limb injury			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Muscle strain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Nasal injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Overdose			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Procedural vomiting			

subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Radius fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Scar			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Scratch			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Skin abrasion			
subjects affected / exposed	1 / 3 (33.33%)	2 / 19 (10.53%)	3 / 12 (25.00%)
occurrences (all)	1	3	6
Skin laceration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Stoma site hypergranulation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Stoma site pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Sunburn			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Thermal burn			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Tongue injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Upper limb fracture			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Venomous sting			

subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Wrist fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Congenital, familial and genetic disorders			
Phimosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Atrioventricular block first degree			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Bradycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Cardiac disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Mitral valve disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Palpitations			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Sinus bradycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Sinus tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	5 / 19 (26.32%)	1 / 12 (8.33%)
occurrences (all)	0	8	1
Systolic dysfunction			

subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Tricuspid valve disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	3
Nervous system disorders			
Allodynia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Aphasia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ataxia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Aura			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Depressed level of consciousness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Disturbance in attention			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Dysarthria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Dyskinesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Facial paralysis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	1 / 3 (33.33%)	11 / 19 (57.89%)	3 / 12 (25.00%)
occurrences (all)	1	15	5
Horner's syndrome			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Hydrocephalus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Memory impairment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Movement disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Muscle spasticity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nystagmus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Sciatica			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Seizure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Visual field defect			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	9 / 19 (47.37%)	6 / 12 (50.00%)
occurrences (all)	0	15	11
Bone marrow oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Eosinophilia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Febrile neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypochromasia			

subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Leukocytosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Leukopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Lymphadenitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Lymphadenopathy			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Lymphopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Thrombocytosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Deafness unilateral			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Ear pain			
subjects affected / exposed	1 / 3 (33.33%)	2 / 19 (10.53%)	2 / 12 (16.67%)
occurrences (all)	2	2	2
External ear inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

External ear pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypoacusis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Middle ear inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Otorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Tympanic membrane perforation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Amblyopia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Astigmatism			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Bell's phenomenon			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Blepharitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	2 / 12 (16.67%)
occurrences (all)	0	1	3
Blindness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Cataract			

subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	1 / 3 (33.33%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Dyschromatopsia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Erythema of eyelid			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Eye discharge			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Eye haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Eye pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Eye swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Eyelid margin crusting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gaze palsy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Heterophoria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypermetropia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Iridocyclitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Keratitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Lacrimation increased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 19 (5.26%)	1 / 12 (8.33%)
occurrences (all)	1	1	1
Mydriasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ocular hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Optic disc disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Optic disc haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Optic nerve disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Periorbital oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pupillary reflex impaired			

subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Retinopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Strabismus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Trichomegaly			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Uveitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Vitreous floaters			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Abdominal mass			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	8 / 19 (42.11%)	7 / 12 (58.33%)
occurrences (all)	0	11	10
Abdominal pain lower			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	1 / 3 (33.33%)	5 / 19 (26.32%)	2 / 12 (16.67%)
occurrences (all)	1	5	2
Anal fissure			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Anal incontinence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Anal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Anal rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Angular cheilitis			
subjects affected / exposed	0 / 3 (0.00%)	4 / 19 (21.05%)	1 / 12 (8.33%)
occurrences (all)	0	5	1
Aphthous ulcer			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Chapped lips			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Cheilitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	3 / 12 (25.00%)
occurrences (all)	0	1	3
Constipation			
subjects affected / exposed	1 / 3 (33.33%)	8 / 19 (42.11%)	6 / 12 (50.00%)
occurrences (all)	1	17	9

Dental caries			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Diarrhoea			
subjects affected / exposed	1 / 3 (33.33%)	17 / 19 (89.47%)	10 / 12 (83.33%)
occurrences (all)	1	41	16
Dry mouth			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Dysphagia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Flatulence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	1 / 12 (8.33%)
occurrences (all)	0	2	1
Gingival bleeding			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gingival erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gingival hypertrophy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gingival oedema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Gingival swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Haematemesis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	2 / 12 (16.67%)
occurrences (all)	0	1	3
Lip blister			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Lip dry			
subjects affected / exposed	0 / 3 (0.00%)	3 / 19 (15.79%)	2 / 12 (16.67%)
occurrences (all)	0	3	3
Lip haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Lip swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Mouth haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	0 / 3 (0.00%)	3 / 19 (15.79%)	0 / 12 (0.00%)
occurrences (all)	0	3	0
Mucous stools			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	6 / 19 (31.58%)	1 / 12 (8.33%)
occurrences (all)	0	11	1
Odynophagia			
subjects affected / exposed	0 / 3 (0.00%)	3 / 19 (15.79%)	1 / 12 (8.33%)
occurrences (all)	0	3	1
Oral disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Oral dysaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Proctalgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	3 / 19 (15.79%)	3 / 12 (25.00%)
occurrences (all)	0	3	12
Teething			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Tooth discolouration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Vomiting			
subjects affected / exposed	1 / 3 (33.33%)	13 / 19 (68.42%)	9 / 12 (75.00%)
occurrences (all)	1	23	14
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ocular icterus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			

Acne			
subjects affected / exposed	1 / 3 (33.33%)	3 / 19 (15.79%)	0 / 12 (0.00%)
occurrences (all)	1	3	0
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	7 / 19 (36.84%)	4 / 12 (33.33%)
occurrences (all)	0	8	4
Blister			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Dermatitis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	2 / 12 (16.67%)
occurrences (all)	0	2	2
Dermatitis acneiform			
subjects affected / exposed	0 / 3 (0.00%)	6 / 19 (31.58%)	4 / 12 (33.33%)
occurrences (all)	0	8	5
Dermatitis atopic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dermatitis diaper			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	1 / 12 (8.33%)
occurrences (all)	0	2	2
Dermatosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	1 / 3 (33.33%)	12 / 19 (63.16%)	10 / 12 (83.33%)
occurrences (all)	1	19	14
Eczema			
subjects affected / exposed	1 / 3 (33.33%)	8 / 19 (42.11%)	5 / 12 (41.67%)
occurrences (all)	1	8	9
Eczema asteatotic			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0

Eczema nummular			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	5 / 19 (26.32%)	1 / 12 (8.33%)
occurrences (all)	0	7	2
Erythema multiforme			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Erythema nodosum			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hair colour changes			
subjects affected / exposed	0 / 3 (0.00%)	3 / 19 (15.79%)	3 / 12 (25.00%)
occurrences (all)	0	3	3
Hair texture abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hand dermatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hyperkeratosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypertrichosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Ingrowing nail			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Intertrigo			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Keratosis pilaris			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Livedo reticularis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Macule			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nail discolouration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Nail disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pain of skin			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Palmar erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Panniculitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Papule			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	1 / 12 (8.33%)
occurrences (all)	0	2	1
Perioral dermatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Petechiae			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Photosensitivity reaction			

subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pigmentation disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Plantar erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Prurigo			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	5 / 19 (26.32%)	1 / 12 (8.33%)
occurrences (all)	0	6	1
Pseudofolliculitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	1 / 3 (33.33%)	9 / 19 (47.37%)	5 / 12 (41.67%)
occurrences (all)	2	18	9
Rash erythematous			
subjects affected / exposed	0 / 3 (0.00%)	3 / 19 (15.79%)	1 / 12 (8.33%)
occurrences (all)	0	3	1
Rash follicular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Rash maculo-papular			
subjects affected / exposed	2 / 3 (66.67%)	3 / 19 (15.79%)	4 / 12 (33.33%)
occurrences (all)	3	4	6
Rash papular			
subjects affected / exposed	0 / 3 (0.00%)	4 / 19 (21.05%)	3 / 12 (25.00%)
occurrences (all)	0	6	4
Rash pruritic			

subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Seborrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Skin burning sensation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Skin depigmentation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Skin disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Skin exfoliation			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	1 / 12 (8.33%)
occurrences (all)	0	2	1
Skin fissures			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Skin fragility			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Skin hypopigmentation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	1 / 3 (33.33%)	2 / 19 (10.53%)	3 / 12 (25.00%)
occurrences (all)	2	2	4
Skin mass			

subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Skin toxicity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Telangiectasia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 12 (8.33%)
occurrences (all)	0	1	2
Renal and urinary disorders			
Albuminuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Crystalluria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Cystitis noninfective			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Glycosuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	4 / 19 (21.05%)	1 / 12 (8.33%)
occurrences (all)	0	10	1
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	4 / 19 (21.05%)	3 / 12 (25.00%)
occurrences (all)	0	14	7
Urethritis noninfective			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	1 / 3 (33.33%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Urinary retention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Urine abnormality			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Adrenocorticotropic hormone deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Growth hormone deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypogonadism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Precocious puberty			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	5 / 19 (26.32%)	2 / 12 (16.67%)
occurrences (all)	0	8	3
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	3 / 19 (15.79%)	2 / 12 (16.67%)
occurrences (all)	0	4	2
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Costochondritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Flank pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Foot deformity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Joint range of motion decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Joint swelling			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Kyphosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Muscle atrophy			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	0 / 12 (0.00%)
occurrences (all)	0	3	0

Muscle swelling			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Musculoskeletal deformity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Neck pain			
subjects affected / exposed	0 / 3 (0.00%)	3 / 19 (15.79%)	2 / 12 (16.67%)
occurrences (all)	0	4	2
Osteoporosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	7 / 19 (36.84%)	3 / 12 (25.00%)
occurrences (all)	0	11	3
Scoliosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Spinal deformity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Spinal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tendonitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Toe walking			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Trismus			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Beta haemolytic streptococcal infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
COVID-19			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	1 / 12 (8.33%)
occurrences (all)	0	2	1
Coronavirus infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Coxsackie viral infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Device related infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Ear infection			

subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	2 / 12 (16.67%)
occurrences (all)	0	2	2
Enterocolitis infectious			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Enterovirus infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Epstein-Barr virus infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Eye infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 12 (8.33%)
occurrences (all)	0	1	2
Folliculitis			
subjects affected / exposed	0 / 3 (0.00%)	6 / 19 (31.58%)	3 / 12 (25.00%)
occurrences (all)	0	10	3
Fungal infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Fungal skin infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Furuncle			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	3 / 19 (15.79%)	0 / 12 (0.00%)
occurrences (all)	0	3	0
Gastroenteritis bacterial			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Gastroenteritis viral			

subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Herpes dermatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Herpes simplex			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Herpes virus infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	0 / 3 (0.00%)	3 / 19 (15.79%)	0 / 12 (0.00%)
occurrences (all)	0	3	0
Impetigo			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Infected bite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Infected skin ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Influenza			

subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	3
Laryngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Localised infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Lymph gland infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Mucosal infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Nail infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nasal vestibulitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Onychomycosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Otitis externa			

subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Otitis media			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	3 / 12 (25.00%)
occurrences (all)	0	1	3
Otitis media acute			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 3 (0.00%)	16 / 19 (84.21%)	10 / 12 (83.33%)
occurrences (all)	0	46	27
Parotitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	3 / 19 (15.79%)	1 / 12 (8.33%)
occurrences (all)	0	3	1
Pharyngitis streptococcal			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	1 / 12 (8.33%)
occurrences (all)	0	4	1
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	2 / 12 (16.67%)
occurrences (all)	0	1	2
Post procedural infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pustule			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Rash pustular			
subjects affected / exposed	1 / 3 (33.33%)	5 / 19 (26.32%)	0 / 12 (0.00%)
occurrences (all)	1	5	0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Respiratory tract infection			

subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Respiratory tract infection bacterial			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	0 / 3 (0.00%)	4 / 19 (21.05%)	0 / 12 (0.00%)
occurrences (all)	0	12	0
Rhinovirus infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Skin bacterial infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Skin candida			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 3 (0.00%)	4 / 19 (21.05%)	2 / 12 (16.67%)
occurrences (all)	0	4	2
Staphylococcal infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Staphylococcal skin infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Stoma site infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tinea capitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tinea faciei			

subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tinea infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Tinea pedis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Tonsillitis			
subjects affected / exposed	0 / 3 (0.00%)	3 / 19 (15.79%)	0 / 12 (0.00%)
occurrences (all)	0	3	0
Tooth infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tracheitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	6 / 19 (31.58%)	3 / 12 (25.00%)
occurrences (all)	0	9	5
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	1 / 12 (8.33%)
occurrences (all)	0	3	1
Varicella			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Viral infection			
subjects affected / exposed	0 / 3 (0.00%)	4 / 19 (21.05%)	1 / 12 (8.33%)
occurrences (all)	0	6	2
Viral pharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Viral rhinitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			

subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Wound sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Alkalosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	2 / 3 (66.67%)	11 / 19 (57.89%)	4 / 12 (33.33%)
occurrences (all)	2	16	4
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	2 / 12 (16.67%)
occurrences (all)	0	2	2
Hyperchloraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	6
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	4 / 19 (21.05%)	3 / 12 (25.00%)
occurrences (all)	0	14	4
Hyperkalaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	1 / 12 (8.33%)
occurrences (all)	0	2	1
Hypermagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Hypernatraemia			
subjects affected / exposed	0 / 3 (0.00%)	5 / 19 (26.32%)	1 / 12 (8.33%)
occurrences (all)	0	6	1
Hyperphosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 3 (33.33%)	5 / 19 (26.32%)	6 / 12 (50.00%)
occurrences (all)	1	16	15

Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	3 / 19 (15.79%)	5 / 12 (41.67%)
occurrences (all)	0	9	9
Hypochloraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	4 / 19 (21.05%)	2 / 12 (16.67%)
occurrences (all)	0	4	5
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	1 / 12 (8.33%)
occurrences (all)	0	2	1
Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	1 / 12 (8.33%)
occurrences (all)	0	3	1
Hypophagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 19 (10.53%)	1 / 12 (8.33%)
occurrences (all)	0	3	3
Hypoproteinaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Obesity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Salt craving			
subjects affected / exposed	0 / 3 (0.00%)	0 / 19 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 3 (0.00%)	1 / 19 (5.26%)	0 / 12 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Part A – TMT 0.04 mg/kg/day	Part B – Neuroblastoma	Part B – LGG fusion
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 16 (100.00%)	11 / 11 (100.00%)	10 / 10 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Neoplasm progression			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Skin papilloma			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tumour pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	1 / 16 (6.25%)	2 / 11 (18.18%)	0 / 10 (0.00%)
occurrences (all)	1	3	0
Hypotension			
subjects affected / exposed	3 / 16 (18.75%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	3	0	2
Lymphoedema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pallor			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1

Surgical and medical procedures			
Central venous catheter removal			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tonsillectomy			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 16 (25.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	5	0	1
Catheter site hypersensitivity			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Catheter site pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Catheter site rash			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Chest discomfort			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Cyst			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Fatigue			

subjects affected / exposed	4 / 16 (25.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	5	2	1
Feeling cold			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Gait disturbance			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Granuloma			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypothermia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Localised oedema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Mucosal inflammation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	4
Non-cardiac chest pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			

subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	10 / 16 (62.50%)	5 / 11 (45.45%)	5 / 10 (50.00%)
occurrences (all)	19	13	8
Swelling face			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ulcer			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Xerosis			
subjects affected / exposed	2 / 16 (12.50%)	1 / 11 (9.09%)	2 / 10 (20.00%)
occurrences (all)	3	1	2
Immune system disorders			
Allergy to arthropod sting			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypersensitivity			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Perineal rash			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal discomfort			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal pruritus			

subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Apnoea			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Aspiration			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	4 / 16 (25.00%)	2 / 11 (18.18%)	4 / 10 (40.00%)
occurrences (all)	6	4	7
Dysphonia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Epistaxis			
subjects affected / exposed	8 / 16 (50.00%)	2 / 11 (18.18%)	2 / 10 (20.00%)
occurrences (all)	12	5	3
Hypoxia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Laryngeal inflammation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Nasal inflammation			

subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Nasal odour			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	4
Pharyngeal swelling			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Productive cough			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Respiratory disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Respiratory tract congestion			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	2 / 10 (20.00%)
occurrences (all)	1	1	2
Sinus congestion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Sneezing			

subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Snoring			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tachypnoea			
subjects affected / exposed	2 / 16 (12.50%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	4	1	2
Throat irritation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Tonsillar hypertrophy			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Agitation			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
Anxiety			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Attention deficit hyperactivity disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Confusional state			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Delirium			

subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Dyssomnia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Enuresis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Initial insomnia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Irritability			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Mood altered			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Obsessive-compulsive disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Restlessness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Alanine aminotransferase increased			

subjects affected / exposed	5 / 16 (31.25%)	2 / 11 (18.18%)	2 / 10 (20.00%)
occurrences (all)	6	6	3
Albumin urine present			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Anion gap decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	7 / 16 (43.75%)	3 / 11 (27.27%)	1 / 10 (10.00%)
occurrences (all)	11	4	4
Bacterial test positive			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood albumin decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 16 (12.50%)	2 / 11 (18.18%)	0 / 10 (0.00%)
occurrences (all)	3	5	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood bicarbonate increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood chloride increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			

subjects affected / exposed	2 / 16 (12.50%)	5 / 11 (45.45%)	1 / 10 (10.00%)
occurrences (all)	3	7	1
Blood glucose increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood urea decreased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Blood urea increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Body temperature fluctuation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Ejection fraction decreased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram ST-T segment abnormal			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram T wave amplitude decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
End-tidal CO2 decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 16 (12.50%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	2	1	0
Grip strength decreased			

subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Haematocrit increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Haemoglobin increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lung diffusion test decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 16 (6.25%)	2 / 11 (18.18%)	0 / 10 (0.00%)
occurrences (all)	1	2	0
Lymphocyte count increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lymphocyte percentage decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	2 / 16 (12.50%)	2 / 11 (18.18%)	1 / 10 (10.00%)
occurrences (all)	5	3	1
Neutrophil percentage increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nitrite urine present			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	2 / 16 (12.50%)	2 / 11 (18.18%)	1 / 10 (10.00%)
occurrences (all)	2	3	3
Protein total decreased			

subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Protein urine			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Red blood cell count decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Red blood cells urine			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Red blood cells urine positive			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Specific gravity urine increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Staphylococcus test positive			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Urine ketone body present			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Urine leukocyte esterase positive			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Urine output decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
Weight increased			
subjects affected / exposed	0 / 16 (0.00%)	2 / 11 (18.18%)	3 / 10 (30.00%)
occurrences (all)	0	3	3
White blood cell count decreased			

subjects affected / exposed	4 / 16 (25.00%)	3 / 11 (27.27%)	1 / 10 (10.00%)
occurrences (all)	6	5	1
White blood cell count increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
White blood cells urine positive			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
pH urine increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	0 / 16 (0.00%)	2 / 11 (18.18%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Fall			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	2
Fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastrostomy tube site complication			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hand fracture			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	2
Head injury			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Incision site pruritus			

subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	3
Muscle strain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nasal injury			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Overdose			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Procedural vomiting			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Radius fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Scar			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Scratch			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Skin laceration			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Stoma site hypergranulation			

subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Stoma site pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sunburn			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Thermal burn			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tongue injury			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Upper limb fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Venomous sting			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Wrist fracture			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Congenital, familial and genetic disorders			
Phimosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Atrioventricular block first degree			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Bradycardia			

subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cardiac disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Mitral valve disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	2 / 16 (12.50%)	2 / 11 (18.18%)	1 / 10 (10.00%)
occurrences (all)	2	4	2
Systolic dysfunction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Tachycardia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Tricuspid valve disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Allodynia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Aphasia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Ataxia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Aura			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Depressed level of consciousness			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Disturbance in attention			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Dysarthria			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dyskinesia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Facial paralysis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	5 / 16 (31.25%)	1 / 11 (9.09%)	4 / 10 (40.00%)
occurrences (all)	7	1	6
Horner's syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hydrocephalus			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0

Lethargy			
subjects affected / exposed	1 / 16 (6.25%)	2 / 11 (18.18%)	0 / 10 (0.00%)
occurrences (all)	1	2	0
Memory impairment			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Movement disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Muscle spasticity			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nystagmus			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Seizure			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	2
Somnolence			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Tremor			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Visual field defect			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 16 (43.75%)	6 / 11 (54.55%)	3 / 10 (30.00%)
occurrences (all)	12	12	5
Bone marrow oedema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eosinophilia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Febrile neutropenia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypochromasia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Leukocytosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lymphadenitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lymphadenopathy			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Lymphopenia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Neutropenia			

subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	2	1	0
Thrombocytopenia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Thrombocytosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Deafness unilateral			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	0	6	1
External ear inflammation			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
External ear pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hypoacusis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Middle ear inflammation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Otorrhoea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tympanic membrane perforation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Eye disorders			
Amblyopia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Astigmatism			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Bell's phenomenon			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blepharitis			
subjects affected / exposed	3 / 16 (18.75%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	4	0	1
Blindness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cataract			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Dry eye			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Dyschromatopsia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Erythema of eyelid			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Eye discharge			
subjects affected / exposed	3 / 16 (18.75%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	3	0	1
Eye haemorrhage			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Eye pain			

subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eye pruritus			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eye swelling			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	3	0
Eyelid margin crusting			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Gaze palsy			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Heterophoria			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypermetropia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Iridocyclitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Keratitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Mydriasis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ocular hypertension			

subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Optic disc disorder			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Optic disc haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Optic nerve disorder			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Periorbital oedema			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Photophobia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pupillary reflex impaired			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Retinopathy			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Strabismus			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Trichomegaly			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Uveitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			

subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Visual impairment			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Vitreous floaters			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Abdominal mass			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	5 / 16 (31.25%)	1 / 11 (9.09%)	5 / 10 (50.00%)
occurrences (all)	9	1	9
Abdominal pain lower			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	2 / 16 (12.50%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	2	1	0
Anal fissure			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Anal incontinence			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	3	1	0
Anal inflammation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Anal rash			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Angular cheilitis			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	1
Aphthous ulcer			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Chapped lips			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cheilitis			
subjects affected / exposed	6 / 16 (37.50%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	6	0	0
Constipation			
subjects affected / exposed	3 / 16 (18.75%)	4 / 11 (36.36%)	5 / 10 (50.00%)
occurrences (all)	4	5	6
Dental caries			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	9 / 16 (56.25%)	6 / 11 (54.55%)	6 / 10 (60.00%)
occurrences (all)	23	6	27
Dry mouth			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Flatulence			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Gingival erythema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Gingival hypertrophy			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Gingival oedema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gingival swelling			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Haematemesis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Haematochezia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lip blister			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lip dry			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	3 / 10 (30.00%)
occurrences (all)	0	0	3
Lip haemorrhage			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Lip swelling			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0

Mouth haemorrhage			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Mouth ulceration			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Mucous stools			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	4 / 16 (25.00%)	3 / 11 (27.27%)	2 / 10 (20.00%)
occurrences (all)	4	4	3
Odynophagia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Oral disorder			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Oral dysaesthesia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Oral pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	2 / 16 (12.50%)	1 / 11 (9.09%)	4 / 10 (40.00%)
occurrences (all)	3	1	7
Teething			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Tooth discolouration			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	6 / 16 (37.50%)	3 / 11 (27.27%)	3 / 10 (30.00%)
occurrences (all)	14	3	15
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Ocular icterus			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Alopecia			
subjects affected / exposed	6 / 16 (37.50%)	1 / 11 (9.09%)	5 / 10 (50.00%)
occurrences (all)	6	1	5
Blister			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Dermatitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	10 / 16 (62.50%)	1 / 11 (9.09%)	4 / 10 (40.00%)
occurrences (all)	21	1	6
Dermatitis atopic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Dermatitis contact			

subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Dermatitis diaper			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dermatosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	6 / 16 (37.50%)	4 / 11 (36.36%)	7 / 10 (70.00%)
occurrences (all)	12	4	7
Eczema			
subjects affected / exposed	9 / 16 (56.25%)	2 / 11 (18.18%)	5 / 10 (50.00%)
occurrences (all)	11	3	7
Eczema asteatotic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eczema nummular			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	5 / 16 (31.25%)	2 / 11 (18.18%)	0 / 10 (0.00%)
occurrences (all)	5	2	0
Erythema multiforme			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Erythema nodosum			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hair colour changes			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	2 / 10 (20.00%)
occurrences (all)	1	1	2
Hair texture abnormal			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Hand dermatitis			

subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hyperkeratosis			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Hypertrichosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ingrowing nail			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Intertrigo			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Keratosis pilaris			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Livedo reticularis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Macule			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Nail discolouration			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nail disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pain of skin			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Palmar erythema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia			

syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Panniculitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Papule			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Perioral dermatitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Petechiae			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Photosensitivity reaction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pigmentation disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Plantar erythema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Prurigo			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	4 / 16 (25.00%)	2 / 11 (18.18%)	1 / 10 (10.00%)
occurrences (all)	5	2	1
Pseudofolliculitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	8 / 16 (50.00%)	4 / 11 (36.36%)	5 / 10 (50.00%)
occurrences (all)	12	6	5

Rash erythematous			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Rash follicular			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Rash macular			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
Rash maculo-papular			
subjects affected / exposed	4 / 16 (25.00%)	2 / 11 (18.18%)	4 / 10 (40.00%)
occurrences (all)	5	2	6
Rash papular			
subjects affected / exposed	3 / 16 (18.75%)	0 / 11 (0.00%)	2 / 10 (20.00%)
occurrences (all)	4	0	6
Rash pruritic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Seborrhoea			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Seborrhoeic dermatitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Skin burning sensation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Skin depigmentation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0

Skin fissures			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	3	0	3
Skin fragility			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin hyperpigmentation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Skin hypopigmentation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	2
Skin mass			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin toxicity			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	4 / 16 (25.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	5	0	0
Telangiectasia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Albuminuria			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Crystalluria			

subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cystitis noninfective			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Glycosuria			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 16 (0.00%)	2 / 11 (18.18%)	1 / 10 (10.00%)
occurrences (all)	0	2	2
Pollakiuria			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Proteinuria			
subjects affected / exposed	2 / 16 (12.50%)	3 / 11 (27.27%)	2 / 10 (20.00%)
occurrences (all)	6	4	7
Urethritis noninfective			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Urinary incontinence			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Urine abnormality			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Adrenocorticotropic hormone deficiency			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Growth hormone deficiency			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypogonadism			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Precocious puberty			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 16 (18.75%)	1 / 11 (9.09%)	2 / 10 (20.00%)
occurrences (all)	6	1	3
Back pain			
subjects affected / exposed	4 / 16 (25.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	4	1	0
Bone pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Costochondritis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Foot deformity			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Groin pain			

subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Joint range of motion decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Kyphosis			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Muscle atrophy			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	3
Muscle swelling			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	2
Musculoskeletal deformity			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Osteoporosis			

subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	3 / 16 (18.75%)	2 / 11 (18.18%)	0 / 10 (0.00%)
occurrences (all)	4	2	0
Scoliosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Spinal deformity			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tendonitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Toe walking			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Trismus			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Beta haemolytic streptococcal infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Candida infection			

subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Cellulitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	4 / 16 (25.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	5	5	2
Coronavirus infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Coxsackie viral infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Device related infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
Enterocolitis infectious			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Enterovirus infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Epstein-Barr virus infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eye infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Folliculitis			

subjects affected / exposed	4 / 16 (25.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	5	0	0
Fungal infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Fungal skin infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Furuncle			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	1
Gastroenteritis bacterial			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Gingivitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Herpes dermatitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Herpes simplex			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Herpes virus infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			

subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Hordeolum			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Impetigo			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Infected bite			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infected skin ulcer			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Laryngitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Localised infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	0	1	2
Lower respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lymph gland infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Mucosal infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nail infection			

subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Nasal vestibulitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Onychomycosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Otitis externa			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Otitis media			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Otitis media acute			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	12 / 16 (75.00%)	0 / 11 (0.00%)	4 / 10 (40.00%)
occurrences (all)	33	0	6
Parotitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pharyngitis streptococcal			

subjects affected / exposed	2 / 16 (12.50%)	1 / 11 (9.09%)	2 / 10 (20.00%)
occurrences (all)	3	1	2
Pneumonia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Post procedural infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pustule			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Rash pustular			
subjects affected / exposed	3 / 16 (18.75%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	5	0	1
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection bacterial			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	2 / 10 (20.00%)
occurrences (all)	3	0	2
Rhinovirus infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Skin bacterial infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin candida			

subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Skin infection			
subjects affected / exposed	3 / 16 (18.75%)	2 / 11 (18.18%)	1 / 10 (10.00%)
occurrences (all)	3	5	2
Staphylococcal infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Staphylococcal skin infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	3
Stoma site infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tinea capitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tinea faciei			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tinea infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Tinea pedis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Tooth infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tracheitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			

subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	1	7	2
Varicella			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Viral infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Viral pharyngitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Viral rhinitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Wound sepsis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Alkalosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	5 / 16 (31.25%)	1 / 11 (9.09%)	3 / 10 (30.00%)
occurrences (all)	6	1	3
Dehydration			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Hyperchloraemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1

Hyperglycaemia			
subjects affected / exposed	4 / 16 (25.00%)	3 / 11 (27.27%)	2 / 10 (20.00%)
occurrences (all)	7	4	12
Hyperkalaemia			
subjects affected / exposed	2 / 16 (12.50%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	5	4	0
Hypermagnesaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Hypernatraemia			
subjects affected / exposed	2 / 16 (12.50%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	2	1	1
Hyperphosphataemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	4 / 16 (25.00%)	4 / 11 (36.36%)	3 / 10 (30.00%)
occurrences (all)	4	6	5
Hypocalcaemia			
subjects affected / exposed	3 / 16 (18.75%)	2 / 11 (18.18%)	1 / 10 (10.00%)
occurrences (all)	6	2	2
Hypochloraemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hypoglycaemia			
subjects affected / exposed	4 / 16 (25.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	4	1	0
Hypokalaemia			
subjects affected / exposed	1 / 16 (6.25%)	2 / 11 (18.18%)	1 / 10 (10.00%)
occurrences (all)	1	3	1
Hypomagnesaemia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 11 (18.18%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Hyponatraemia			
subjects affected / exposed	1 / 16 (6.25%)	3 / 11 (27.27%)	1 / 10 (10.00%)
occurrences (all)	1	4	1

Hypophagia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Hypophosphataemia			
subjects affected / exposed	1 / 16 (6.25%)	3 / 11 (27.27%)	1 / 10 (10.00%)
occurrences (all)	1	10	1
Hypoproteinaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Obesity			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Salt craving			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part B – NF-1 with PN	Part B – BRAF V600 mutant solid tumor	Part C – TMT 0.025 mg/kg/day + 50% DRB RP2D
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)	10 / 10 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neoplasm progression			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin papilloma			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tumour pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			

Flushing			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypotension			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Lymphoedema			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Pallor			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Central venous catheter removal			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tonsillectomy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Catheter site hypersensitivity			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Catheter site pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Catheter site rash			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Chest pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Cyst			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Face oedema			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 10 (0.00%)	6 / 10 (60.00%)	2 / 3 (66.67%)
occurrences (all)	0	10	3
Feeling cold			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Gait disturbance			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Granuloma			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypothermia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Localised oedema			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	1 / 10 (10.00%)	3 / 10 (30.00%)	1 / 3 (33.33%)
occurrences (all)	2	4	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Pain			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Peripheral swelling			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	6 / 10 (60.00%)	4 / 10 (40.00%)	0 / 3 (0.00%)
occurrences (all)	14	9	0
Swelling face			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ulcer			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Xerosis			
subjects affected / exposed	1 / 10 (10.00%)	3 / 10 (30.00%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Immune system disorders			
Allergy to arthropod sting			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Hypersensitivity			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Perineal rash			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal discomfort			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal pruritus			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Respiratory, thoracic and mediastinal disorders			
Apnoea			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Aspiration			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	5 / 10 (50.00%)	4 / 10 (40.00%)	1 / 3 (33.33%)
occurrences (all)	7	5	1
Dysphonia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Dyspnoea exertional			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	1 / 3 (33.33%)
occurrences (all)	1	3	1
Hypoxia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Laryngeal inflammation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	3 / 10 (30.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	3	1	0
Nasal inflammation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal odour			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 10 (10.00%)	3 / 10 (30.00%)	1 / 3 (33.33%)
occurrences (all)	1	4	1
Pharyngeal swelling			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Respiratory disorder			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory tract congestion			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Rhinorrhoea			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Sinus congestion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sleep apnoea syndrome			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Sneezing			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Snoring			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Tachypnoea			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Throat irritation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tonsillar hypertrophy			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Wheezing			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Agitation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Attention deficit hyperactivity disorder			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Delirium			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dyssomnia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Enuresis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Initial insomnia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Irritability			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Mood altered			

subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Obsessive-compulsive disorder			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Restlessness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Albumin urine present			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Anion gap decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 10 (10.00%)	6 / 10 (60.00%)	1 / 3 (33.33%)
occurrences (all)	1	8	1
Bacterial test positive			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood albumin decreased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood bicarbonate decreased			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood bicarbonate increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood chloride increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood glucose increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood urea decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Body temperature fluctuation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ejection fraction decreased			
subjects affected / exposed	0 / 10 (0.00%)	3 / 10 (30.00%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram ST-T segment abnormal			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram T wave amplitude decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
End-tidal CO2 decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	1 / 3 (33.33%)
occurrences (all)	0	6	2
Grip strength decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haematocrit increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Haemoglobin increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lung diffusion test decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Lymphocyte count increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lymphocyte percentage decreased			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neutrophil percentage increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nitrite urine present			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Protein total decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Protein urine			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Red blood cell count decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Red blood cells urine			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Red blood cells urine positive			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Specific gravity urine increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Staphylococcus test positive			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urine ketone body present			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urine leukocyte esterase positive			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urine output decreased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Weight increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
White blood cell count decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
White blood cells urine positive			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
pH urine increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Contusion			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Fall			

subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Fracture			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrostomy tube site complication			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hand fracture			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Head injury			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Incision site pruritus			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle strain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal injury			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Overdose			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Procedural pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Procedural vomiting			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Radius fracture			

subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Scar			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Scratch			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Skin laceration			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Stoma site hypergranulation			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Stoma site pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sunburn			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Thermal burn			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Tongue injury			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Upper limb fracture			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Venomous sting			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Wrist fracture			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Phimosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Atrioventricular block first degree			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bradycardia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac disorder			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mitral valve disease			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Palpitations			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Systolic dysfunction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tachycardia			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tricuspid valve disease			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Allodynia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Aphasia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ataxia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Aura			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Depressed level of consciousness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Disturbance in attention			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Dysarthria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dyskinesia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Facial paralysis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	4 / 10 (40.00%)	3 / 10 (30.00%)	1 / 3 (33.33%)
occurrences (all)	7	9	7
Horner's syndrome			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hydrocephalus			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypoaesthesia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Lethargy			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Memory impairment			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Movement disorder			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Muscle spasticity			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nystagmus			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Sciatica			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Seizure			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Somnolence			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Visual field defect			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 10 (40.00%)	5 / 10 (50.00%)	0 / 3 (0.00%)
occurrences (all)	4	9	0
Bone marrow oedema			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eosinophilia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Febrile neutropenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypochromasia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Leukocytosis			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Lymphadenitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lymphadenopathy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Thrombocytopenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Thrombocytosis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Deafness unilateral			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
External ear inflammation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
External ear pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Hypoacusis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Middle ear inflammation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Otorrhoea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tympanic membrane perforation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Amblyopia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Astigmatism			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bell's phenomenon			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blepharitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blindness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cataract			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry eye			

subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dyschromatopsia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Erythema of eyelid			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye discharge			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye pruritus			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye swelling			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eyelid margin crusting			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gaze palsy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Heterophoria			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypermetropia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Iridocyclitis			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Keratitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mydriasis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ocular hypertension			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Optic disc disorder			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Optic disc haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Optic nerve disorder			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pupillary reflex impaired			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Retinopathy			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Strabismus			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Trichomegaly			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Uveitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	5
Vision blurred			
subjects affected / exposed	2 / 10 (20.00%)	1 / 10 (10.00%)	1 / 3 (33.33%)
occurrences (all)	2	1	1
Visual acuity reduced			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vitreous floaters			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal mass			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	0 / 3 (0.00%)
occurrences (all)	1	4	0

Abdominal pain lower			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Anal fissure			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Anal incontinence			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Anal inflammation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Anal rash			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Angular cheilitis			
subjects affected / exposed	0 / 10 (0.00%)	3 / 10 (30.00%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Aphthous ulcer			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Chapped lips			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cheilitis			
subjects affected / exposed	2 / 10 (20.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Constipation			
subjects affected / exposed	2 / 10 (20.00%)	6 / 10 (60.00%)	1 / 3 (33.33%)
occurrences (all)	2	7	1
Dental caries			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Diarrhoea			
subjects affected / exposed	5 / 10 (50.00%)	6 / 10 (60.00%)	2 / 3 (66.67%)
occurrences (all)	13	11	4
Dry mouth			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Dysphagia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gingival bleeding			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gingival erythema			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gingival hypertrophy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gingival oedema			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gingival swelling			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haematemesis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Haematochezia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lip blister			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lip dry			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Lip haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lip swelling			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mouth haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Mucous stools			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	3 / 10 (30.00%)	3 / 10 (30.00%)	0 / 3 (0.00%)
occurrences (all)	6	4	0
Odynophagia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral disorder			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral dysaesthesia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Oral pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	3 / 10 (30.00%)	2 / 10 (20.00%)	0 / 3 (0.00%)
occurrences (all)	3	4	0
Teething			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tooth discolouration			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	3 / 10 (30.00%)	6 / 10 (60.00%)	1 / 3 (33.33%)
occurrences (all)	10	16	1
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ocular icterus			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Alopecia			

subjects affected / exposed	4 / 10 (40.00%)	3 / 10 (30.00%)	0 / 3 (0.00%)
occurrences (all)	4	3	0
Blister			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dermatitis			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Dermatitis acneiform			
subjects affected / exposed	3 / 10 (30.00%)	4 / 10 (40.00%)	2 / 3 (66.67%)
occurrences (all)	3	6	2
Dermatitis atopic			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis diaper			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Dermatosis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dry skin			
subjects affected / exposed	5 / 10 (50.00%)	6 / 10 (60.00%)	2 / 3 (66.67%)
occurrences (all)	7	9	3
Eczema			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Eczema asteatotic			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Eczema nummular			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Erythema			

subjects affected / exposed	0 / 10 (0.00%)	3 / 10 (30.00%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Erythema multiforme			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Erythema nodosum			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hair colour changes			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Hair texture abnormal			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hand dermatitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hyperkeratosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypertrichosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ingrowing nail			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Intertrigo			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Keratosis pilaris			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Livedo reticularis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Macule			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nail discolouration			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nail disorder			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Pain of skin			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Palmar erythema			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Panniculitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Papule			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Perioral dermatitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Petechiae			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Photosensitivity reaction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pigmentation disorder			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1

Plantar erythema			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Prurigo			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	1 / 10 (10.00%)	3 / 10 (30.00%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Pseudofolliculitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	6 / 10 (60.00%)	2 / 10 (20.00%)	3 / 3 (100.00%)
occurrences (all)	6	4	4
Rash erythematous			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Rash follicular			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	2 / 10 (20.00%)	3 / 10 (30.00%)	1 / 3 (33.33%)
occurrences (all)	4	4	1
Rash papular			
subjects affected / exposed	0 / 10 (0.00%)	4 / 10 (40.00%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Rash pruritic			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Seborrhoea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Seborrhoeic dermatitis			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Skin burning sensation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin depigmentation			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Skin disorder			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Skin exfoliation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin fissures			
subjects affected / exposed	1 / 10 (10.00%)	3 / 10 (30.00%)	0 / 3 (0.00%)
occurrences (all)	4	3	0
Skin fragility			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Skin hypopigmentation			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Skin lesion			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	4	1	0
Skin mass			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin toxicity			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

Skin ulcer			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Telangiectasia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Renal and urinary disorders			
Albuminuria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Crystalluria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cystitis noninfective			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Glycosuria			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Haematuria			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Pollakiuria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 10 (0.00%)	3 / 10 (30.00%)	0 / 3 (0.00%)
occurrences (all)	0	12	0
Urethritis noninfective			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urine abnormality			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Adrenocorticotropic hormone deficiency			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Growth hormone deficiency			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypogonadism			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hypothyroidism			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Precocious puberty			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Back pain			

subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Bone pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Costochondritis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Foot deformity			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint range of motion decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Kyphosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle atrophy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Muscle swelling			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal deformity			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Neck pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Osteoporosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	0 / 3 (0.00%)
occurrences (all)	3	2	0
Scoliosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Spinal deformity			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Tendonitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Toe walking			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Trismus			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Beta haemolytic streptococcal infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Coronavirus infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Coxsackie viral infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Device related infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Ear infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Enterocolitis infectious			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Enterovirus infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Epstein-Barr virus infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	2 / 10 (20.00%)	2 / 10 (20.00%)	0 / 3 (0.00%)
occurrences (all)	4	5	0
Fungal infection			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Fungal skin infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Furuncle			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Gastroenteritis bacterial			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal infection			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Herpes dermatitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Herpes simplex			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Herpes virus infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Herpes zoster			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Impetigo			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infected bite			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Infected skin ulcer			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Laryngitis			

subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Localised infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Lower respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lymph gland infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Mucosal infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nail infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal vestibulitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Onychomycosis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Otitis externa			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Otitis media			

subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Otitis media acute			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	7 / 10 (70.00%)	7 / 10 (70.00%)	2 / 3 (66.67%)
occurrences (all)	14	14	6
Parotitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pharyngitis streptococcal			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Post procedural infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pustule			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash pustular			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection bacterial			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	3 / 10 (30.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	8	1	0
Rhinovirus infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Skin bacterial infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin candida			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Staphylococcal infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Staphylococcal skin infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Stoma site infection			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Tinea capitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Tinea faciei			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Tinea infection			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tinea pedis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Tracheitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	3 / 10 (30.00%)	3 / 10 (30.00%)	0 / 3 (0.00%)
occurrences (all)	3	5	0
Urinary tract infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Varicella			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Viral pharyngitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Viral rhinitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Wound sepsis			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Alkalosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	2 / 10 (20.00%)	3 / 10 (30.00%)	0 / 3 (0.00%)
occurrences (all)	3	5	0
Dehydration			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperchloraemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	0 / 3 (0.00%)
occurrences (all)	1	11	0
Hyperkalaemia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypermagnesaemia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypernatraemia			
subjects affected / exposed	0 / 10 (0.00%)	3 / 10 (30.00%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Hyperphosphataemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 10 (10.00%)	3 / 10 (30.00%)	0 / 3 (0.00%)
occurrences (all)	1	9	0
Hypocalcaemia			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	0 / 3 (0.00%)
occurrences (all)	1	8	0

Hypochloraemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Hypokalaemia			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Hypomagnesaemia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hyponatraemia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Hypophagia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Hypoproteinaemia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Obesity			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Salt craving			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part C – TMT 0.025 mg/kg/day + 100% DRB RP2D	Part C – TMT 0.032 mg/kg/day + 100% DRB RP2D	Part D – LGG
Total subjects affected by non-serious			

adverse events			
subjects affected / exposed	9 / 9 (100.00%)	6 / 6 (100.00%)	20 / 20 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Neoplasm progression			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Skin papilloma			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Tumour pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	2 / 20 (10.00%)
occurrences (all)	1	0	2
Haematoma			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Hypertension			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	2 / 9 (22.22%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	5	0	0
Lymphoedema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pallor			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Surgical and medical procedures			

Central venous catheter removal			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Tonsillectomy			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Catheter site hypersensitivity			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Catheter site pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Catheter site rash			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Chills			
subjects affected / exposed	3 / 9 (33.33%)	0 / 6 (0.00%)	3 / 20 (15.00%)
occurrences (all)	8	0	10
Cyst			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Fatigue			

subjects affected / exposed	4 / 9 (44.44%)	1 / 6 (16.67%)	9 / 20 (45.00%)
occurrences (all)	9	2	10
Feeling cold			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Granuloma			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hypothermia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Influenza like illness			
subjects affected / exposed	1 / 9 (11.11%)	2 / 6 (33.33%)	2 / 20 (10.00%)
occurrences (all)	1	4	3
Localised oedema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Mucosal inflammation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	2
Non-cardiac chest pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	3 / 20 (15.00%)
occurrences (all)	0	0	3
Pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Peripheral swelling			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	7 / 9 (77.78%)	4 / 6 (66.67%)	15 / 20 (75.00%)
occurrences (all)	23	10	45
Swelling face			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Ulcer			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Xerosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Allergy to arthropod sting			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hypersensitivity			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Perineal rash			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal discomfort			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal pruritus			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Apnoea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Aspiration			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	4 / 9 (44.44%)	1 / 6 (16.67%)	8 / 20 (40.00%)
occurrences (all)	6	1	14
Dysphonia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Dyspnoea exertional			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	2 / 9 (22.22%)	0 / 6 (0.00%)	2 / 20 (10.00%)
occurrences (all)	2	0	3
Hypoxia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Laryngeal inflammation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	2 / 9 (22.22%)	1 / 6 (16.67%)	5 / 20 (25.00%)
occurrences (all)	3	1	6
Nasal inflammation			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nasal odour			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	3 / 9 (33.33%)	0 / 6 (0.00%)	3 / 20 (15.00%)
occurrences (all)	3	0	4
Pharyngeal swelling			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Respiratory disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Respiratory tract congestion			
subjects affected / exposed	2 / 9 (22.22%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	2
Rhinorrhoea			
subjects affected / exposed	3 / 9 (33.33%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	3	0	0
Sinus congestion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Sneezing			

subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Snoring			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Tachypnoea			
subjects affected / exposed	3 / 9 (33.33%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	7	0	0
Throat irritation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tonsillar hypertrophy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Agitation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Anxiety			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Attention deficit hyperactivity disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Delirium			

subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Dyssomnia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Enuresis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Initial insomnia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Irritability			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Mood altered			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Obsessive-compulsive disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Restlessness			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			

subjects affected / exposed	1 / 9 (11.11%)	1 / 6 (16.67%)	3 / 20 (15.00%)
occurrences (all)	1	1	4
Albumin urine present			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Anion gap decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 9 (33.33%)	3 / 6 (50.00%)	5 / 20 (25.00%)
occurrences (all)	4	3	9
Bacterial test positive			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood albumin decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 9 (22.22%)	2 / 6 (33.33%)	2 / 20 (10.00%)
occurrences (all)	3	2	5
Blood bicarbonate decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood bicarbonate increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood chloride increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			

subjects affected / exposed	2 / 9 (22.22%)	2 / 6 (33.33%)	0 / 20 (0.00%)
occurrences (all)	8	2	0
Blood glucose increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood urea decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Body temperature fluctuation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Ejection fraction decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	3	0	0
Electrocardiogram ST-T segment abnormal			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram T wave amplitude decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
End-tidal CO2 decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 9 (22.22%)	2 / 6 (33.33%)	3 / 20 (15.00%)
occurrences (all)	2	3	4
Grip strength decreased			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Haematocrit increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Haemoglobin increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	3
Lung diffusion test decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	2 / 9 (22.22%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	2	0	2
Lymphocyte count increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lymphocyte percentage decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	3 / 9 (33.33%)	0 / 6 (0.00%)	3 / 20 (15.00%)
occurrences (all)	8	0	5
Neutrophil percentage increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nitrite urine present			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Platelet count decreased			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Protein total decreased			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Protein urine			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Red blood cell count decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Red blood cells urine			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Red blood cells urine positive			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Specific gravity urine increased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Staphylococcus test positive			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Urine ketone body present			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Urine leukocyte esterase positive			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Urine output decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	1 / 9 (11.11%)	2 / 6 (33.33%)	5 / 20 (25.00%)
occurrences (all)	1	2	7
White blood cell count decreased			

subjects affected / exposed	2 / 9 (22.22%)	0 / 6 (0.00%)	3 / 20 (15.00%)
occurrences (all)	4	0	6
White blood cell count increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	2
White blood cells urine positive			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
pH urine increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Contusion			
subjects affected / exposed	1 / 9 (11.11%)	1 / 6 (16.67%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Fall			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Gastrostomy tube site complication			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hand fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Head injury			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Incision site pruritus			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Muscle strain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nasal injury			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Overdose			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Procedural vomiting			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Radius fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Scar			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Scratch			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Skin laceration			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Stoma site hypergranulation			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Stoma site pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Sunburn			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Thermal burn			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tongue injury			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Upper limb fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Venomous sting			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Wrist fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Phimosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Atrioventricular block first degree			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Bradycardia			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cardiac disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Mitral valve disease			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	2 / 20 (10.00%)
occurrences (all)	1	0	2
Sinus tachycardia			
subjects affected / exposed	3 / 9 (33.33%)	0 / 6 (0.00%)	2 / 20 (10.00%)
occurrences (all)	6	0	2
Systolic dysfunction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	2 / 9 (22.22%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	3	0	1
Tricuspid valve disease			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Allodynia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Aphasia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Ataxia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Aura			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Depressed level of consciousness			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Disturbance in attention			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	3 / 9 (33.33%)	0 / 6 (0.00%)	4 / 20 (20.00%)
occurrences (all)	6	0	6
Dysarthria			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Dysgeusia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dyskinesia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Facial paralysis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	4 / 9 (44.44%)	1 / 6 (16.67%)	9 / 20 (45.00%)
occurrences (all)	6	1	13
Horner's syndrome			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hydrocephalus			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Lethargy			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Memory impairment			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Movement disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Muscle spasticity			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nystagmus			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	3 / 9 (33.33%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	6	0	1
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Seizure			
subjects affected / exposed	1 / 9 (11.11%)	1 / 6 (16.67%)	1 / 20 (5.00%)
occurrences (all)	1	2	1
Somnolence			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Visual field defect			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 9 (44.44%)	1 / 6 (16.67%)	4 / 20 (20.00%)
occurrences (all)	7	1	9
Bone marrow oedema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Eosinophilia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Febrile neutropenia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Hypochromasia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Leukocytosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lymphadenitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lymphadenopathy			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Lymphopenia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Neutropenia			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	3 / 20 (15.00%)
occurrences (all)	0	0	4
Thrombocytopenia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Thrombocytosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Deafness unilateral			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
External ear inflammation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
External ear pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hypoacusis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Middle ear inflammation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Otorrhoea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tympanic membrane perforation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Vertigo			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Eye disorders			
Amblyopia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Astigmatism			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Bell's phenomenon			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blepharitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Blindness			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cataract			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dyschromatopsia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Erythema of eyelid			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Eye discharge			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Eye haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Eye pain			

subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Eye pruritus			
subjects affected / exposed	2 / 9 (22.22%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Eye swelling			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Eyelid margin crusting			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gaze palsy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Heterophoria			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Hypermetropia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Iridocyclitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Keratitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Mydriasis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Ocular hyperaemia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Ocular hypertension			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Optic disc disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Optic disc haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Optic nerve disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pupillary reflex impaired			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Retinopathy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Strabismus			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Trichomegaly			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Uveitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Visual acuity reduced			

subjects affected / exposed	1 / 9 (11.11%)	1 / 6 (16.67%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Visual impairment			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Vitreous floaters			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Abdominal mass			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	3 / 9 (33.33%)	2 / 6 (33.33%)	6 / 20 (30.00%)
occurrences (all)	6	2	9
Abdominal pain lower			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Anal fissure			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Anal incontinence			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Anal inflammation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Anal rash			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Angular cheilitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	2 / 20 (10.00%)
occurrences (all)	2	0	2
Aphthous ulcer			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Chapped lips			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cheilitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	2 / 20 (10.00%)
occurrences (all)	1	0	2
Constipation			
subjects affected / exposed	2 / 9 (22.22%)	1 / 6 (16.67%)	5 / 20 (25.00%)
occurrences (all)	4	1	6
Dental caries			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	3 / 9 (33.33%)	3 / 6 (50.00%)	7 / 20 (35.00%)
occurrences (all)	7	5	18
Dry mouth			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 9 (22.22%)	0 / 6 (0.00%)	2 / 20 (10.00%)
occurrences (all)	2	0	2
Gingival bleeding			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gingival erythema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gingival hypertrophy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gingival oedema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gingival swelling			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Haematemesis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lip blister			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lip dry			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Lip haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lip swelling			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Mouth haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Mucous stools			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	4 / 9 (44.44%)	1 / 6 (16.67%)	8 / 20 (40.00%)
occurrences (all)	9	1	14
Odynophagia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Oral disorder			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Oral dysaesthesia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	2 / 9 (22.22%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	2	0	2
Teething			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Tooth discolouration			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	4 / 9 (44.44%)	4 / 6 (66.67%)	9 / 20 (45.00%)
occurrences (all)	6	5	18
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Ocular icterus			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	3 / 20 (15.00%)
occurrences (all)	0	1	3
Alopecia			
subjects affected / exposed	1 / 9 (11.11%)	1 / 6 (16.67%)	1 / 20 (5.00%)
occurrences (all)	2	1	1
Blister			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Dermatitis acneiform			
subjects affected / exposed	4 / 9 (44.44%)	1 / 6 (16.67%)	8 / 20 (40.00%)
occurrences (all)	5	1	12
Dermatitis atopic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dermatitis diaper			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dermatosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	5 / 9 (55.56%)	3 / 6 (50.00%)	8 / 20 (40.00%)
occurrences (all)	7	4	10
Eczema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	3 / 20 (15.00%)
occurrences (all)	0	0	4
Eczema asteatotic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Eczema nummular			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	2 / 20 (10.00%)
occurrences (all)	1	0	2
Erythema multiforme			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Erythema nodosum			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Hair colour changes			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Hair texture abnormal			
subjects affected / exposed	1 / 9 (11.11%)	1 / 6 (16.67%)	1 / 20 (5.00%)
occurrences (all)	1	1	1
Hand dermatitis			

subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Hyperkeratosis			
subjects affected / exposed	2 / 9 (22.22%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	2	0	1
Hypertrichosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Ingrowing nail			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Intertrigo			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Keratosis pilaris			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Livedo reticularis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Macule			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Nail discolouration			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nail disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pain of skin			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Palmar erythema			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Palmar-plantar erythrodysaesthesia			

syndrome			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	2
Panniculitis			
subjects affected / exposed	1 / 9 (11.11%)	1 / 6 (16.67%)	1 / 20 (5.00%)
occurrences (all)	3	2	3
Papule			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Perioral dermatitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Petechiae			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Photosensitivity reaction			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Pigmentation disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Plantar erythema			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Prurigo			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	2 / 9 (22.22%)	0 / 6 (0.00%)	3 / 20 (15.00%)
occurrences (all)	3	0	3
Pseudofolliculitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	6 / 9 (66.67%)	2 / 6 (33.33%)	3 / 20 (15.00%)
occurrences (all)	10	2	3

Rash erythematous			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	3 / 20 (15.00%)
occurrences (all)	0	1	5
Rash follicular			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Rash macular			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Rash maculo-papular			
subjects affected / exposed	0 / 9 (0.00%)	2 / 6 (33.33%)	6 / 20 (30.00%)
occurrences (all)	0	2	12
Rash papular			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	2 / 20 (10.00%)
occurrences (all)	1	0	3
Rash pruritic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Seborrhoea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Skin burning sensation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Skin depigmentation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Skin disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1

Skin fissures			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Skin fragility			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Skin hyperpigmentation			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	2	0	1
Skin hypopigmentation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	2 / 20 (10.00%)
occurrences (all)	1	0	3
Skin mass			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	2
Skin toxicity			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Telangiectasia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	3 / 20 (15.00%)
occurrences (all)	0	0	5
Renal and urinary disorders			
Albuminuria			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Crystalluria			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cystitis noninfective			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	2 / 20 (10.00%)
occurrences (all)	1	0	2
Glycosuria			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Haematuria			
subjects affected / exposed	4 / 9 (44.44%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	8	0	1
Pollakiuria			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	3 / 9 (33.33%)	2 / 6 (33.33%)	1 / 20 (5.00%)
occurrences (all)	11	2	1
Urethritis noninfective			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Urine abnormality			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Adrenocorticotropic hormone deficiency			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Growth hormone deficiency			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Hypogonadism			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Precocious puberty			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 9 (44.44%)	0 / 6 (0.00%)	4 / 20 (20.00%)
occurrences (all)	4	0	4
Back pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Bone pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Costochondritis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Flank pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Foot deformity			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Groin pain			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Joint range of motion decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Kyphosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Muscle atrophy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Muscle swelling			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	2 / 9 (22.22%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal deformity			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	2 / 9 (22.22%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	4	0	1
Neck pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Osteoporosis			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	3 / 20 (15.00%)
occurrences (all)	1	0	3
Scoliosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Spinal deformity			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tendonitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Toe walking			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Trismus			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Beta haemolytic streptococcal infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Candida infection			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Cellulitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Coronavirus infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Coxsackie viral infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Device related infection			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Ear infection			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	2
Enterocolitis infectious			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Enterovirus infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Epstein-Barr virus infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Escherichia urinary tract infection			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Eye infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Folliculitis			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Fungal infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Fungal skin infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Furuncle			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Gastroenteritis bacterial			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	2 / 9 (22.22%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Gastrointestinal infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Herpes dermatitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Herpes simplex			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Herpes virus infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Impetigo			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Infected bite			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Infected skin ulcer			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Localised infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Lymph gland infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Mucosal infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Nail infection			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nasal vestibulitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	3 / 20 (15.00%)
occurrences (all)	0	1	3
Onychomycosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Otitis externa			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Otitis media acute			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Paronychia			
subjects affected / exposed	1 / 9 (11.11%)	1 / 6 (16.67%)	6 / 20 (30.00%)
occurrences (all)	1	1	11
Parotitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	3 / 20 (15.00%)
occurrences (all)	0	0	4
Pharyngitis streptococcal			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	2
Pneumonia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Post procedural infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pustule			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Rash pustular			
subjects affected / exposed	1 / 9 (11.11%)	1 / 6 (16.67%)	1 / 20 (5.00%)
occurrences (all)	1	1	1
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection bacterial			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	2 / 9 (22.22%)	0 / 6 (0.00%)	2 / 20 (10.00%)
occurrences (all)	2	0	2
Rhinovirus infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Skin bacterial infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Skin candida			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	1 / 20 (5.00%)
occurrences (all)	0	2	1
Staphylococcal infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Staphylococcal skin infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Stoma site infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tinea capitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tinea faciei			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tinea infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tinea pedis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Tooth infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tracheitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			

subjects affected / exposed	2 / 9 (22.22%)	1 / 6 (16.67%)	6 / 20 (30.00%)
occurrences (all)	3	1	8
Urinary tract infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Varicella			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	1 / 9 (11.11%)	1 / 6 (16.67%)	1 / 20 (5.00%)
occurrences (all)	1	1	1
Viral pharyngitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Viral rhinitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Wound sepsis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Alkalosis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Decreased appetite			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	4 / 20 (20.00%)
occurrences (all)	1	0	4
Dehydration			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Hyperchloraemia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0

Hyperglycaemia			
subjects affected / exposed	3 / 9 (33.33%)	0 / 6 (0.00%)	4 / 20 (20.00%)
occurrences (all)	11	0	12
Hyperkalaemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	2
Hypermagnesaemia			
subjects affected / exposed	2 / 9 (22.22%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	5	0	1
Hypernatraemia			
subjects affected / exposed	2 / 9 (22.22%)	1 / 6 (16.67%)	2 / 20 (10.00%)
occurrences (all)	6	1	2
Hyperphosphataemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	4 / 9 (44.44%)	2 / 6 (33.33%)	3 / 20 (15.00%)
occurrences (all)	12	4	6
Hypocalcaemia			
subjects affected / exposed	4 / 9 (44.44%)	0 / 6 (0.00%)	2 / 20 (10.00%)
occurrences (all)	15	0	2
Hypochloraemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	3 / 9 (33.33%)	1 / 6 (16.67%)	0 / 20 (0.00%)
occurrences (all)	7	1	0
Hypokalaemia			
subjects affected / exposed	2 / 9 (22.22%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	2	0	1
Hypomagnesaemia			
subjects affected / exposed	2 / 9 (22.22%)	1 / 6 (16.67%)	4 / 20 (20.00%)
occurrences (all)	3	3	6
Hyponatraemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Hypophagia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Hypophosphataemia			
subjects affected / exposed	1 / 9 (11.11%)	1 / 6 (16.67%)	3 / 20 (15.00%)
occurrences (all)	2	1	5
Hypoproteinaemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Obesity			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Salt craving			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Part D – LCH		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Neoplasm progression			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Skin papilloma			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Tumour pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Vascular disorders			

Flushing			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		
Haematoma			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Lymphoedema			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pallor			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Surgical and medical procedures			
Central venous catheter removal			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Tonsillectomy			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Catheter site hypersensitivity			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Catheter site pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Catheter site rash			

subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Chest discomfort				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Chest pain				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Chills				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Cyst				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Face oedema				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Fatigue				
subjects affected / exposed	4 / 10 (40.00%)			
occurrences (all)	4			
Feeling cold				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Gait disturbance				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Granuloma				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Hypothermia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Influenza like illness				
subjects affected / exposed	3 / 10 (30.00%)			
occurrences (all)	6			
Localised oedema				

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Malaise			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Mucosal inflammation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Non-cardiac chest pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Peripheral swelling			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	8 / 10 (80.00%)		
occurrences (all)	26		
Swelling face			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Ulcer			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Xerosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Allergy to arthropod sting			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		

Hypersensitivity			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Perineal rash			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Vulvovaginal discomfort			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Vulvovaginal pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Vulvovaginal pruritus			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Apnoea			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Aspiration			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	6 / 10 (60.00%)		
occurrences (all)	6		
Dysphonia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Dyspnoea exertional			

subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Epistaxis				
subjects affected / exposed	3 / 10 (30.00%)			
occurrences (all)	8			
Hypoxia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Laryngeal inflammation				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Nasal congestion				
subjects affected / exposed	3 / 10 (30.00%)			
occurrences (all)	3			
Nasal inflammation				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Nasal odour				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Oropharyngeal pain				
subjects affected / exposed	2 / 10 (20.00%)			
occurrences (all)	2			
Pharyngeal swelling				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Pleural effusion				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Productive cough				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Respiratory disorder				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Respiratory tract congestion				

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Rhinitis allergic			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Sinus congestion			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Sleep apnoea syndrome			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Sneezing			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Snoring			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Tachypnoea			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Throat irritation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Tonsillar hypertrophy			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Wheezing			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		

Agitation				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Anxiety				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Attention deficit hyperactivity disorder				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Confusional state				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Delirium				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Depression				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Dyssomnia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Enuresis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Initial insomnia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Insomnia				
subjects affected / exposed	2 / 10 (20.00%)			
occurrences (all)	2			
Irritability				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Mood altered				

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Obsessive-compulsive disorder			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Restlessness			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Alanine aminotransferase increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Albumin urine present			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Anion gap decreased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Bacterial test positive			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood albumin decreased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Blood bicarbonate decreased			

subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Blood bicarbonate increased				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Blood chloride increased				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Blood creatine phosphokinase increased				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Blood creatinine increased				
subjects affected / exposed	2 / 10 (20.00%)			
occurrences (all)	2			
Blood glucose increased				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Blood urea decreased				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Blood urea increased				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Body temperature fluctuation				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Ejection fraction decreased				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Electrocardiogram QT prolonged				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Electrocardiogram ST-T segment abnormal				

subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Electrocardiogram T wave amplitude decreased				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
End-tidal CO2 decreased				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Gamma-glutamyltransferase increased				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Grip strength decreased				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Haematocrit increased				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Haemoglobin decreased				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Haemoglobin increased				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Lung diffusion test decreased				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Lymphocyte count decreased				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Lymphocyte count increased				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Lymphocyte percentage decreased				

subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Neutrophil count decreased				
subjects affected / exposed	5 / 10 (50.00%)			
occurrences (all)	8			
Neutrophil percentage increased				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Nitrite urine present				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Platelet count decreased				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Protein total decreased				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Protein urine				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Red blood cell count decreased				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Red blood cells urine				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Red blood cells urine positive				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Specific gravity urine increased				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Staphylococcus test positive				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Urine ketone body present				

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Urine leukocyte esterase positive			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Urine output decreased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Weight increased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
White blood cell count decreased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
White blood cell count increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
White blood cells urine positive			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
pH urine increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Fall			

subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Fracture				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Gastrostomy tube site complication				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Hand fracture				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Head injury				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Incision site pruritus				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Limb injury				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Muscle strain				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Nasal injury				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Overdose				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Procedural pain				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Procedural vomiting				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Radius fracture				

subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Scar				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Scratch				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Skin abrasion				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Skin laceration				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Stoma site hypergranulation				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Stoma site pain				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Sunburn				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Thermal burn				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Tongue injury				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Upper limb fracture				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Venomous sting				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Wrist fracture				

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Congenital, familial and genetic disorders			
Phimosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Atrioventricular block first degree			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Bradycardia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Cardiac disorder			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Mitral valve disease			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Palpitations			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Sinus bradycardia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Sinus tachycardia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Systolic dysfunction			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Tachycardia			

subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Tricuspid valve disease			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Allodynia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Aphasia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Ataxia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Aura			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Depressed level of consciousness			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Disturbance in attention			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		
Dysarthria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dysgeusia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dyskinesia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		

Facial paralysis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Headache				
subjects affected / exposed	2 / 10 (20.00%)			
occurrences (all)	3			
Horner's syndrome				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Hydrocephalus				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Hypoaesthesia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Lethargy				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Memory impairment				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Movement disorder				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Muscle spasticity				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Nystagmus				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Paraesthesia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Peripheral sensory neuropathy				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			

Sciatica				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Seizure				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Somnolence				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Syncope				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Tremor				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Visual field defect				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	2 / 10 (20.00%)			
occurrences (all)	2			
Bone marrow oedema				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Eosinophilia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Febrile neutropenia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Hypochromasia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Leukocytosis				

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Leukopenia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Lymphadenitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Lymphadenopathy			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Lymphopenia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Neutropenia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Thrombocytopenia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Thrombocytosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Deafness unilateral			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Ear pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
External ear inflammation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
External ear pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		

Hypoacusis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Middle ear inflammation				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Otorrhoea				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Tympanic membrane perforation				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Vertigo				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Eye disorders				
Amblyopia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Astigmatism				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Bell's phenomenon				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Blepharitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Blindness				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Cataract				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Dry eye				

subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Dyschromatopsia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Erythema of eyelid				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Eye discharge				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Eye haemorrhage				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Eye pain				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Eye pruritus				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Eye swelling				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Eyelid margin crusting				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Gaze palsy				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Heterophoria				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Hypermetropia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Iridocyclitis				

subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Keratitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Lacrimation increased				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Mydriasis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Ocular hyperaemia				
subjects affected / exposed	2 / 10 (20.00%)			
occurrences (all)	2			
Ocular hypertension				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Optic disc disorder				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Optic disc haemorrhage				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Optic nerve disorder				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Periorbital oedema				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Photophobia				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Pupillary reflex impaired				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Retinopathy				

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Strabismus			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Trichomegaly			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Uveitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Vision blurred			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Visual acuity reduced			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Visual impairment			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Vitreous floaters			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Abdominal distension			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Abdominal mass			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	4 / 10 (40.00%)		
occurrences (all)	4		

Abdominal pain lower				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Abdominal pain upper				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Anal fissure				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Anal incontinence				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Anal inflammation				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Anal rash				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Angular cheilitis				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Aphthous ulcer				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Chapped lips				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Cheilitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Constipation				
subjects affected / exposed	2 / 10 (20.00%)			
occurrences (all)	2			
Dental caries				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			

Diarrhoea				
subjects affected / exposed	5 / 10 (50.00%)			
occurrences (all)	7			
Dry mouth				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Dyspepsia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Dysphagia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Flatulence				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Gastrooesophageal reflux disease				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Gingival bleeding				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Gingival erythema				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Gingival hypertrophy				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Gingival oedema				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Gingival swelling				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Haematemesis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			

Haematochezia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Lip blister				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Lip dry				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Lip haemorrhage				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Lip swelling				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Mouth haemorrhage				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Mouth ulceration				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Mucous stools				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Nausea				
subjects affected / exposed	3 / 10 (30.00%)			
occurrences (all)	4			
Odynophagia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Oral disorder				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Oral dysaesthesia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			

Oral pain subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Proctalgia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Rectal haemorrhage subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Stomatitis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Teething subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Tooth discolouration subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Toothache subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Vomiting subjects affected / exposed occurrences (all)	7 / 10 (70.00%) 11		
Hepatobiliary disorders Jaundice subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Ocular icterus subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Alopecia			

subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Blister				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Dermatitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Dermatitis acneiform				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Dermatitis atopic				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Dermatitis contact				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Dermatitis diaper				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Dermatosis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Dry skin				
subjects affected / exposed	5 / 10 (50.00%)			
occurrences (all)	5			
Eczema				
subjects affected / exposed	2 / 10 (20.00%)			
occurrences (all)	2			
Eczema asteatotic				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Eczema nummular				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Erythema				

subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	2			
Erythema multiforme				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Erythema nodosum				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Hair colour changes				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Hair texture abnormal				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Hand dermatitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Hyperkeratosis				
subjects affected / exposed	2 / 10 (20.00%)			
occurrences (all)	3			
Hypertrichosis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Ingrowing nail				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Intertrigo				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Keratosis pilaris				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Livedo reticularis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Macule				

subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Nail discolouration				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Nail disorder				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Pain of skin				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Palmar erythema				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Palmar-plantar erythrodysaesthesia syndrome				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Panniculitis				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Papule				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Perioral dermatitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Petechiae				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Photosensitivity reaction				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Pigmentation disorder				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			

Plantar erythema				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Prurigo				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Pruritus				
subjects affected / exposed	3 / 10 (30.00%)			
occurrences (all)	3			
Pseudofolliculitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Rash				
subjects affected / exposed	2 / 10 (20.00%)			
occurrences (all)	3			
Rash erythematous				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Rash follicular				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Rash macular				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Rash maculo-papular				
subjects affected / exposed	5 / 10 (50.00%)			
occurrences (all)	7			
Rash papular				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Rash pruritic				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Seborrhoea				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			

Seborrhoeic dermatitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Skin burning sensation				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Skin depigmentation				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Skin disorder				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Skin exfoliation				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Skin fissures				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Skin fragility				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Skin hyperpigmentation				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Skin hypopigmentation				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Skin lesion				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Skin mass				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Skin toxicity				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			

Skin ulcer			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Telangiectasia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Urticaria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Albuminuria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Crystalluria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cystitis noninfective			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Dysuria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Glycosuria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Haematuria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pollakiuria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Proteinuria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Urethritis noninfective			

subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Urinary incontinence subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Urinary retention subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Urine abnormality subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Endocrine disorders			
Adrenal insufficiency subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Adrenocorticotropic hormone deficiency subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Growth hormone deficiency subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Hypogonadism subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Hypothyroidism subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Precocious puberty subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Back pain			

subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Bone pain				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Costochondritis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Flank pain				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Foot deformity				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Groin pain				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Joint range of motion decreased				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Joint swelling				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Kyphosis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Muscle atrophy				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Muscle spasms				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Muscle swelling				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Muscular weakness				

subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Musculoskeletal deformity				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Musculoskeletal pain				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Myalgia				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Neck pain				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Osteoporosis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Pain in extremity				
subjects affected / exposed	4 / 10 (40.00%)			
occurrences (all)	5			
Scoliosis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Spinal deformity				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Spinal pain				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Tendonitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Toe walking				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Trismus				

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Beta haemolytic streptococcal infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Bronchitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
COVID-19			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Candida infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cellulitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Conjunctivitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Coronavirus infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Coxsackie viral infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Device related infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Ear infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Enterocolitis infectious			

subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Enterovirus infection				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Epstein-Barr virus infection				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Escherichia urinary tract infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Eye infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Folliculitis				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Fungal infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Fungal skin infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Furuncle				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Gastroenteritis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Gastroenteritis bacterial				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Gastroenteritis viral				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Gastrointestinal infection				

subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Gingivitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Herpes dermatitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Herpes simplex				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Herpes virus infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Herpes zoster				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Hordeolum				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Impetigo				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Infected bite				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Infected skin ulcer				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Infection				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Influenza				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Laryngitis				

subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Localised infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Lower respiratory tract infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Lymph gland infection				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Mucosal infection				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Nail infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Nasal vestibulitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Nasopharyngitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Onychomycosis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Oral candidiasis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Oral herpes				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Otitis externa				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Otitis media				

subjects affected / exposed	2 / 10 (20.00%)			
occurrences (all)	2			
Otitis media acute				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Paronychia				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Parotitis				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	2			
Pharyngitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Pharyngitis streptococcal				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Pneumonia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Post procedural infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Pustule				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Rash pustular				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Respiratory syncytial virus infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Respiratory tract infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Respiratory tract infection bacterial				

subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Rhinitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Rhinovirus infection				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Sinusitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Skin bacterial infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Skin candida				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Skin infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Staphylococcal infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Staphylococcal skin infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Stoma site infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Tinea capitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Tinea faciei				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Tinea infection				

subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Tinea pedis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Tonsillitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Tooth infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Tracheitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Upper respiratory tract infection				
subjects affected / exposed	4 / 10 (40.00%)			
occurrences (all)	5			
Urinary tract infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Varicella				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Viral infection				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Viral pharyngitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Viral rhinitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Viral upper respiratory tract infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Wound sepsis				

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Alkalosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Decreased appetite			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dehydration			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hyperchloraemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hyperkalaemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypermagnesaemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypernatraemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hyperphosphataemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypoalbuminaemia			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Hypocalcaemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		

Hypochloraemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Hypoglycaemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Hypokalaemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Hypomagnesaemia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Hyponatraemia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Hypophagia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Hypophosphataemia subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 3		
Hypoproteinaemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Obesity subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Salt craving subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Vitamin D deficiency subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 March 2014	Subjects must have been less than 18 years of age to enroll. Part B Leukemia cohort was removed. Part B cohort B1 was restricted to subjects with relapsed or refractory neuroblastoma and Part B cohort B4 was added to allow subjects with BRAF V600 mutant solid tumors to be treated with trametinib monotherapy. Guidelines and dose modifications for trametinib events of special interest were updated and RANO criteria were added for disease response assessment for CNS tumors.
14 April 2015	Eligibility criteria was revised to clarify that subjects with NF-1 associated PNs and subjects with LCH were eligible. At the request of regulatory, the timeframe for pregnancy testing prior to enrollment was shortened from 14 to 7 days in applicable subjects. Exclusion criteria were changed to exclude only optic pathway tumors that were being actively treated. Cardiovascular exclusion criteria were updated to be consistent with requirements in other dabrafenib and trametinib studies; Removal of RPED (retinal pigment epithelium detachment) as an exclusion criterion, based on current safety data that only requires history of RVO (retinal vein occlusion) as an exclusion; Removal of heparin-sensitivity as an exclusion as there are no known drug-drug interactions between heparin and trametinib or dabrafenib. MRIs were required in Part B for PN subjects. Updated to clarify that there were no prohibited medications in Parts A and B.
05 January 2016	This amendment was made to expand the description of Part C to include the dabrafenib RP2D levels and rationale along with the observed safety in pediatric subjects on dabrafenib monotherapy. Updated safety information from adult combination studies was included.
20 September 2016	Subsequent to the acquisition of GlaxoSmithKline (GSK) compound GSK1120212 and GSK2118436 by Novartis, the purpose of this protocol Amendment 4 was to delete or replace references to GSK or its staff with that of Novartis and its authorized agents to align with the change of sponsorship and to make administrative changes to align with Novartis processes and procedures.
08 March 2017	The purpose of this amendment was to add 2 new specific BRAF V600 mutant disease cohorts (LGG and LCH) for study combination therapy of dabrafenib and trametinib to obtain preliminary efficacy information in these diseases, as well as additional safety, tolerability and PK data for the combination. The 2 dose escalation portions of the protocol (Part A and Part C) were extended to allow additional dose exploration of trametinib in subjects under 6 years of age in an effort to obtain target exposure comparable to adults in this age group.
17 September 2018	The purpose of this amendment was the addition of a new pediatric formulation dosage form of dabrafenib 10 mg as dispersible tablets and to update the withdrawal of consent language to align with the new Global Data Protection Requirements.
04 April 2019	The purpose of this amendment was to add additional interim analyses of data to support health authority requests/publication requests.
23 January 2020	The main purpose of this amendment was to add dose modification requirements for cases of severe cutaneous adverse reactions (SCARs) which had been reported during treatment with dabrafenib in combination with trametinib outside this clinical study. The definition of 'Study Completion' was also amended, reducing the minimum treatment duration from 12 months to 6 months. Dabrafenib powder for oral suspension (150 mg stickpack, 10 mg/mL in oral suspension), and trametinib 0.125 mg tablets were removed, as the manufacturing of these formulations was discontinued. Subjects were changed to dabrafenib 10 mg dispersible tablets and trametinib 0.5 mg and 2 mg tablets.

21 August 2020	The purpose of this amendment was to add updated RANO criteria specifically for low grade glioma as the basis for independent review. These more recent RANO-LGG criteria allowed for the identification of measurable target lesions in subjects with LGG that may not be gadolinium enhancing and are best seen by T2/FLAIR imaging sequences. These updated RANO - LGG criteria were utilized in supplemental independent RANO response determination for those subjects with LGG. this study. In addition, the contraception information was updated following results from a trametinib PK study which showed that no loss of efficacy of combined hormonal contraceptives (norethindrone and ethinyl estradiol) was expected when co-administered with trametinib monotherapy.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com for complete trial results.

Notes: