



Clinical trial results:

A Phase 1 Study to Evaluate the Safety and Pharmacokinetics of Panitumumab in Children with Solid Tumors

Summary

EudraCT number	2014-005190-36
Trial protocol	Outside EU/EEA
Global end of trial date	25 March 2015

Results information

Result version number	v1 (current)
This version publication date	29 May 2016
First version publication date	29 May 2016

Trial information

Trial identification

Sponsor protocol code	20050252
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00658658
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States, 91320
Public contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com
Scientific contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 March 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	25 March 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the safety and pharmacokinetics of up to 3 different dose schedules of panitumumab in pediatric patients with solid tumors.

Protection of trial subjects:

This study was conducted in accordance with ICH GCP regulations/guidelines.

All subjects provided written informed consent before undergoing any study-related procedures, including screening procedures.

The study protocol, amendments, and the informed consent form (ICF) were reviewed by the Institutional Review Boards (IRBs) and Independent Ethics Committees (IECs). No subjects were recruited into the study and no investigational product (IP) was shipped until the IRB/IEC gave written approval of the protocol and ICF and Amgen received copies of these approvals.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 March 2008
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: 31
Worldwide total number of subjects	31
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	14
Adolescents (12-17 years)	17
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 7 centers in the United States. Participants were enrolled from 14 March 2008 to 4 March 2015.

Pre-assignment

Screening details:

Three dose regimens were to be tested in pediatric patients stratified by age group (1 to 11 versus 12 to 17 years). Participants were enrolled sequentially into each dose group, beginning with the 2.5 mg/kg, 12 to 17 year old cohort, based upon demonstration of sufficient safety.

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	Age 12–17: 2.5 mg/kg QW

Arm description:

Participants aged 12 to 17 years received panitumumab 2.5 mg/kg administered by intravenous (IV) infusion weekly (QW) until the participant experienced disease progression, was unable to tolerate study drug, withdrew consent, or other reasons that warranted removal from the study.

Arm type	Experimental
Investigational medicinal product name	Panitumumab
Investigational medicinal product code	
Other name	Vectibix
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Panitumumab administered by intravenous infusion over 60 minutes for doses \leq 1000 mg and over 60 to 90 minutes for doses $>$ 1000 mg.

Arm title	Age 12–17: 6 mg/kg Q2W
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Arm description:

Participants aged 12 to 17 years received panitumumab 6 mg/kg administered by IV infusion every 2 weeks (Q2W) until the participant experienced disease progression, was unable to tolerate study drug, withdrew consent, or other reasons that warranted removal from the study.

Arm type	Experimental
Investigational medicinal product name	Panitumumab
Investigational medicinal product code	
Other name	Vectibix
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Panitumumab administered by intravenous infusion over 60 minutes for doses \leq 1000 mg and over 60 to 90 minutes for doses $>$ 1000 mg.

Arm title	Age 12–17: 9 mg/kg Q3W
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Arm description:

Participants aged 12 to 17 years received panitumumab 9 mg/kg administered by IV infusion every 3 weeks (Q3W) until the participant experienced disease progression, was unable to tolerate study drug, withdrew consent, or other reasons that warranted removal from the study.

Arm type	Experimental
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Investigational medicinal product name	Panitumumab
Investigational medicinal product code	
Other name	Vectibix
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Panitumumab administered by intravenous infusion over 60 minutes for doses \leq 1000 mg and over 60 to 90 minutes for doses $>$ 1000 mg.

Arm title	Age 1–11: 2.5 mg/kg QW
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Arm description:

Participants aged 1 to 11 years received panitumumab 2.5 mg/kg administered by IV infusion QW until the participant experienced disease progression, was unable to tolerate study drug, withdrew consent, or other reasons that warranted removal from the study.

Arm type	Experimental
Investigational medicinal product name	Panitumumab
Investigational medicinal product code	
Other name	Vectibix
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Panitumumab administered by intravenous infusion over 60 minutes for doses \leq 1000 mg and over 60 to 90 minutes for doses $>$ 1000 mg.

Arm title	Age 1–11: 6 mg/kg Q2W
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Arm description:

Participants aged 1 to 11 years received panitumumab 6 mg/kg administered by IV infusion Q2W until the participant experienced disease progression, was unable to tolerate study drug, withdrew consent, or other reasons that warranted removal from the study.

Arm type	Experimental
Investigational medicinal product name	Panitumumab
Investigational medicinal product code	
Other name	Vectibix
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Panitumumab administered by intravenous infusion over 60 minutes for doses \leq 1000 mg and over 60 to 90 minutes for doses $>$ 1000 mg.

Number of subjects in period 1	Age 12–17: 2.5 mg/kg QW	Age 12–17: 6 mg/kg Q2W	Age 12–17: 9 mg/kg Q3W
Started	6	7	4
Completed	1	5	4
Not completed	5	2	0
Consent withdrawn by subject	-	1	-
Death	4	-	-
Other	-	-	-
Protocol-specified Criteria	1	-	-
Disease Progression	-	1	-

Number of subjects in period 1	Age 1–11: 2.5 mg/kg QW	Age 1–11: 6 mg/kg Q2W
Started	6	8
Completed	4	3
Not completed	2	5
Consent withdrawn by subject	-	-
Death	1	1
Other	-	1
Protocol-specified Criteria	-	-
Disease Progression	1	3

Baseline characteristics

Reporting groups

Reporting group title	Age 12–17: 2.5 mg/kg QW
Reporting group description: Participants aged 12 to 17 years received panitumumab 2.5 mg/kg administered by intravenous (IV) infusion weekly (QW) until the participant experienced disease progression, was unable to tolerate study drug, withdrew consent, or other reasons that warranted removal from the study.	
Reporting group title	Age 12–17: 6 mg/kg Q2W
Reporting group description: Participants aged 12 to 17 years received panitumumab 6 mg/kg administered by IV infusion every 2 weeks (Q2W) until the participant experienced disease progression, was unable to tolerate study drug, withdrew consent, or other reasons that warranted removal from the study.	
Reporting group title	Age 12–17: 9 mg/kg Q3W
Reporting group description: Participants aged 12 to 17 years received panitumumab 9 mg/kg administered by IV infusion every 3 weeks (Q3W) until the participant experienced disease progression, was unable to tolerate study drug, withdrew consent, or other reasons that warranted removal from the study.	
Reporting group title	Age 1–11: 2.5 mg/kg QW
Reporting group description: Participants aged 1 to 11 years received panitumumab 2.5 mg/kg administered by IV infusion QW until the participant experienced disease progression, was unable to tolerate study drug, withdrew consent, or other reasons that warranted removal from the study.	
Reporting group title	Age 1–11: 6 mg/kg Q2W
Reporting group description: Participants aged 1 to 11 years received panitumumab 6 mg/kg administered by IV infusion Q2W until the participant experienced disease progression, was unable to tolerate study drug, withdrew consent, or other reasons that warranted removal from the study.	

Reporting group values	Age 12–17: 2.5 mg/kg QW	Age 12–17: 6 mg/kg Q2W	Age 12–17: 9 mg/kg Q3W
Number of subjects	6	7	4
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0–27 days)	0	0	0
Infants and toddlers (28 days–23 months)	0	0	0
Children (2–11 years)	0	0	0
Adolescents (12–17 years)	6	7	4
Adults (18–64 years)	0	0	0
From 65–84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	13.2	15.6	15.8
standard deviation	± 0.8	± 1.5	± 1.9
Gender, Male/Female Units: participants			
Female	3	1	3
Male	3	6	1

Race/Ethnicity, Customized Units: Subjects			
Asian	0	2	0
Black (or African American)	1	1	0
Hispanic or Latino	0	0	1
Other	0	0	0
White or Caucasian	5	4	3

Reporting group values	Age 1-11: 2.5 mg/kg QW	Age 1-11: 6 mg/kg Q2W	Total
Number of subjects	6	8	31
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	6	8	14
Adolescents (12-17 years)	0	0	17
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	7.8	8.4	
standard deviation	± 3.1	± 2.8	-
Gender, Male/Female Units: participants			
Female	3	4	14
Male	3	4	17
Race/Ethnicity, Customized Units: Subjects			
Asian	0	0	2
Black (or African American)	1	0	3
Hispanic or Latino	0	1	2
Other	1	0	1
White or Caucasian	4	7	23

End points

End points reporting groups

Reporting group title	Age 12–17: 2.5 mg/kg QW
Reporting group description: Participants aged 12 to 17 years received panitumumab 2.5 mg/kg administered by intravenous (IV) infusion weekly (QW) until the participant experienced disease progression, was unable to tolerate study drug, withdrew consent, or other reasons that warranted removal from the study.	
Reporting group title	Age 12–17: 6 mg/kg Q2W
Reporting group description: Participants aged 12 to 17 years received panitumumab 6 mg/kg administered by IV infusion every 2 weeks (Q2W) until the participant experienced disease progression, was unable to tolerate study drug, withdrew consent, or other reasons that warranted removal from the study.	
Reporting group title	Age 12–17: 9 mg/kg Q3W
Reporting group description: Participants aged 12 to 17 years received panitumumab 9 mg/kg administered by IV infusion every 3 weeks (Q3W) until the participant experienced disease progression, was unable to tolerate study drug, withdrew consent, or other reasons that warranted removal from the study.	
Reporting group title	Age 1–11: 2.5 mg/kg QW
Reporting group description: Participants aged 1 to 11 years received panitumumab 2.5 mg/kg administered by IV infusion QW until the participant experienced disease progression, was unable to tolerate study drug, withdrew consent, or other reasons that warranted removal from the study.	
Reporting group title	Age 1–11: 6 mg/kg Q2W
Reporting group description: Participants aged 1 to 11 years received panitumumab 6 mg/kg administered by IV infusion Q2W until the participant experienced disease progression, was unable to tolerate study drug, withdrew consent, or other reasons that warranted removal from the study.	

Primary: Number of Participants with Dose-limiting Toxicities (DLTs)

End point title	Number of Participants with Dose-limiting Toxicities (DLTs) ^[1]
End point description: Any panitumumab related grade 3 or 4 hematologic or non-hematologic toxicity (graded according to the modified Common Terminology Criteria for Adverse Events (CTCAE) version 3.0 criteria) was considered a DLT with the exception of alopecia and fatigue. Hypomagnesemia, nausea, diarrhea, vomiting, and skin or nail toxicities constituted a DLT only if the following occurred: <ul style="list-style-type: none">• Grade 3 or 4 hypomagnesemia that persisted for at least 5 days despite maximal magnesium replacement;• Grade 3 or 4 diarrhea, nausea, or vomiting that persisted for at least 5 days despite maximum supportive therapy;• Grade 4 skin or nail toxicity. This analysis was performed in the DLT Analysis Set which included all participants who received at least 1 dose of panitumumab and were evaluated for DLTs and completed at least 28 days (for the 2.5 and 6 mg/kg cohorts) or 21 days (for 9 mg/kg cohort) of therapy unless due to a DLT.	
End point type	Primary
End point timeframe: 28 days from initial administration of panitumumab for the 2.5 and 6 mg/kg cohorts and 21 days from first administration for the 9 mg/kg cohort.	
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: A formal hypothesis was not tested in this study. All results are descriptive in nature.	

End point values	Age 12–17: 2.5 mg/kg QW	Age 12–17: 6 mg/kg Q2W	Age 12–17: 9 mg/kg Q3W	Age 1–11: 2.5 mg/kg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	5	4	4
Units: participants				
number (not applicable)	1	0	0	1

End point values	Age 1–11: 6 mg/kg Q2W			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: participants				
number (not applicable)	3			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Adverse Events (AEs)

End point title	Number of Participants with Adverse Events (AEs) ^[2]
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End point description:

A serious adverse event is defined as an AE that:

- is fatal;
- is life threatening;
- requires in-patient hospitalization or prolongation of existing hospitalization;
- results in persistent or significant disability/incapacity;
- is a congenital anomaly/birth defect;
- other significant medical hazard.

The investigator assessed whether adverse events were related to panitumumab. The severity of adverse events was based on CTCAE version 3 (with the exception of skin- or nail-related toxicities which were graded using the CTCAE version 3.0 with modifications), according to the following: Grade 1 = Mild (aware of sign or symptom, but easily tolerated); Grade 2 = Moderate (discomfort enough to cause interference with usual activity); Grade 3 = Severe (incapacitating with inability to work or do usual activity); Grade 4 = Life-threatening or disabling; Grade 5 = Fatal.

Adverse event analyses include all participants who received at least one dose of panitumumab.

End point type	Primary
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End point timeframe:

From first dose date to end of study date. The median duration of study was 47 days.

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: A formal hypothesis was not tested in this study. All results are descriptive in nature.

End point values	Age 12–17: 2.5 mg/kg QW	Age 12–17: 6 mg/kg Q2W	Age 12–17: 9 mg/kg Q3W	Age 1–11: 2.5 mg/kg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	7	4	6
Units: participants				
number (not applicable)				
Any adverse event	6	7	3	6
Serious adverse events	5	3	2	3

Treatment-related adverse event	5	5	3	5
Treatment-related serious adverse event	1	0	0	1
Withdrawals due to adverse event	0	0	0	0
Grade 1	5	7	3	6
Grade 2	5	6	3	4
Grade 3	4	5	2	4
Grade 4	4	0	0	1
Fatal	4	0	0	1

End point values	Age 1–11: 6 mg/kg Q2W			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: participants				
number (not applicable)				
Any adverse event	8			
Serious adverse events	5			
Treatment-related adverse event	6			
Treatment-related serious adverse event	2			
Withdrawals due to adverse event	0			
Grade 1	6			
Grade 2	7			
Grade 3	6			
Grade 4	2			
Fatal	1			

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Observed Concentration (Cmax) of Panitumumab

End point title	Maximum Observed Concentration (Cmax) of Panitumumab ^[3]
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End point description:

Panitumumab serum concentration was measured using an enzyme-linked immunosorbent assay (ELISA). The lower limit of quantification (LLOQ) of the assay was 400 pg/mL. Concentrations below the LLOQ were set to zero.

The Pharmacokinetic (PK) Analysis Set included all participants who received the correct dose of panitumumab and from whom the PK parameters could be assessed; "n" indicates the number of participants with available data for each time point.

Standard deviation was not calculated when n < 3; "99999" is entered as a placeholder.

End point type	Primary
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End point timeframe:

First dose (Day 1) and third dose (Day 15/29/43 for the QW, Q2W and Q3W cohorts respectively). Samples were collected over the dosing interval for each treatment cohort (7, 14 or 21 days for QW, Q2W and Q3W cohorts respectively).

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: A formal hypothesis was not tested in this study. All results are descriptive in nature.

End point values	Age 12–17: 2.5 mg/kg QW	Age 12–17: 6 mg/kg Q2W	Age 12–17: 9 mg/kg Q3W	Age 1–11: 2.5 mg/kg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	7	3	4
Units: µg/mL				
arithmetic mean (standard deviation)				
First Dose (n=6, 7, 3, 4, 7)	52.8 (± 11.4)	161 (± 41.2)	205 (± 45.9)	42.9 (± 8.51)
Third Dose (n=3, 5, 1, 3, 2)	76.6 (± 21.1)	187 (± 45.2)	327 (± 99999)	60.8 (± 15.7)

End point values	Age 1–11: 6 mg/kg Q2W			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: µg/mL				
arithmetic mean (standard deviation)				
First Dose (n=6, 7, 3, 4, 7)	120 (± 29.4)			
Third Dose (n=3, 5, 1, 3, 2)	126 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Primary: Minimum Observed Concentration (Cmin) of Panitumumab

End point title	Minimum Observed Concentration (Cmin) of Panitumumab ^[4]
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End point description:

Standard deviation was not calculated when n < 3; "99999" is entered as a placeholder.

End point type	Primary
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End point timeframe:

First dose (Day 1) and third dose (Day 15/29/43 for the QW, Q2W and Q3W cohorts respectively). Samples were collected over the dosing interval for each treatment cohort (7, 14 or 21 days for QW, Q2W and Q3W cohorts respectively).

Notes:

[4] - 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: A formal hypothesis was not tested in this study. All results are descriptive in nature.

End point values	Age 12–17: 2.5 mg/kg QW	Age 12–17: 6 mg/kg Q2W	Age 12–17: 9 mg/kg Q3W	Age 1–11: 2.5 mg/kg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	7	2	4
Units: µg/mL				
arithmetic mean (standard deviation)				
First Dose (n=4, 7, 2, 4, 5)	6.62 (± 6.83)	24.7 (± 18.6)	35.3 (± 99999)	4.87 (± 3.64)

Third Dose (n=3, 5, 0, 3, 2)	24.2 (± 22.9)	48.1 (± 25.1)	99999 (± 99999)	17.3 (± 8.83)
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End point values	Age 1–11: 6 mg/kg Q2W			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: µg/mL				
arithmetic mean (standard deviation)				
First Dose (n=4, 7, 2, 4, 5)	19.7 (± 15.5)			
Third Dose (n=3, 5, 0, 3, 2)	26.1 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Concentration-time Curve During the Dosing Interval (AUC0-tau) for Panitumumab

End point title	Area Under the Concentration-time Curve During the Dosing Interval (AUC0-tau) for Panitumumab ^[5]
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End point description:

The area under the serum concentration-time curve from time zero to the end of the dosing interval (AUCtau), estimated using the linear trapezoidal method.

Standard deviation was not calculated when n < 3; "99999" is entered as a placeholder.

End point type	Primary
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End point timeframe:

First dose (Day 1) and third dose (Day 15/29/43 for the QW, Q2W and Q3W cohorts respectively). Samples were collected over the dosing interval for each treatment cohort (7, 14 or 21 days for QW, Q2W and Q3W cohorts respectively).

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: A formal hypothesis was not tested in this study. All results are descriptive in nature.

End point values	Age 12–17: 2.5 mg/kg QW	Age 12–17: 6 mg/kg Q2W	Age 12–17: 9 mg/kg Q3W	Age 1–11: 2.5 mg/kg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	7	2	4
Units: day*µg/mL				
arithmetic mean (standard deviation)				
First Dose (n=4, 7, 2, 4, 5)	167 (± 86.1)	1040 (± 357)	1580 (± 99999)	127 (± 37.9)
Third Dose (n=3, 5, 0, 3, 2)	306 (± 178)	1330 (± 357)	99999 (± 99999)	255 (± 70.7)

End point values	Age 1–11: 6 mg/kg Q2W			
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Subject group type	Reporting group			
Number of subjects analysed	5			
Units: day*µg/mL				
arithmetic mean (standard deviation)				
First Dose (n=4, 7, 2, 4, 5)	708 (± 247)			
Third Dose (n=3, 5, 0, 3, 2)	754 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Primary: Half-life (t1/2) for the Terminal Phase (First Dose) or Dosing Interval (Third Dose) of Panitumumab

End point title	Half-life (t1/2) for the Terminal Phase (First Dose) or Dosing Interval (Third Dose) of Panitumumab ^[6]
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End point description:

Standard deviation was not calculated when n < 3; "99999" is entered as placeholder.

End point type	Primary
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End point timeframe:

First dose (Day 1) and third dose (Day 15/29/43 for the QW, Q2W and Q3W cohorts respectively). Samples were collected over the dosing interval for each treatment cohort (7, 14 or 21 days for QW, Q2W and Q3W cohorts respectively).

Notes:

[6] - 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: A formal hypothesis was not tested in this study. All results are descriptive in nature.

End point values	Age 12–17: 2.5 mg/kg QW	Age 12–17: 6 mg/kg Q2W	Age 12–17: 9 mg/kg Q3W	Age 1–11: 2.5 mg/kg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	5	1	3
Units: days				
arithmetic mean (standard deviation)				
First Dose (n=2, 5, 1, 3, 3)	1.33 (± 99999)	4.49 (± 1.09)	4.27 (± 99999)	2.11 (± 0.913)
Third Dose (n=2, 2, 0, 1, 1)	2.94 (± 99999)	4.98 (± 99999)	99999 (± 99999)	3.07 (± 99999)

End point values	Age 1–11: 6 mg/kg Q2W			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: days				
arithmetic mean (standard deviation)				
First Dose (n=2, 5, 1, 3, 3)	4.23 (± 1.64)			
Third Dose (n=2, 2, 0, 1, 1)	4.91 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Primary: Serum Clearance (CL) of Panitumumab

End point title	Serum Clearance (CL) of Panitumumab ^[7]
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End point description:

Standard deviation was not calculated when $n < 3$; "99999" is entered as a placeholder.

End point type	Primary
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End point timeframe:

First dose (Day 1) and third dose (Day 15/29/43 for the QW, Q2W and Q3W cohorts respectively). Samples were collected over the dosing interval for each treatment cohort (7, 14 or 21 days for QW, Q2W and Q3W cohorts respectively).

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: A formal hypothesis was not tested in this study. All results are descriptive in nature.

End point values	Age 12–17: 2.5 mg/kg QW	Age 12–17: 6 mg/kg Q2W	Age 12–17: 9 mg/kg Q3W	Age 1–11: 2.5 mg/kg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	5	1	4
Units: mL/day/kg				
arithmetic mean (standard deviation)				
First Dose (n=3, 5, 1, 4, 3)	19.8 (± 8.57)	6.38 (± 0.466)	7.15 (± 99999)	18.7 (± 6.35)
Third Dose (n=3, 5, 0, 3, 2)	9.92 (± 4.4)	4.69 (± 1)	99999 (± 99999)	10.1 (± 2.44)

End point values	Age 1–11: 6 mg/kg Q2W			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: mL/day/kg				
arithmetic mean (standard deviation)				
First Dose (n=3, 5, 1, 4, 3)	8.06 (± 1.4)			
Third Dose (n=3, 5, 0, 3, 2)	8.05 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Developed Antibodies to Panitumumab

End point title	Number of Participants who Developed Antibodies to Panitumumab
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End point description:

Three validated assays were used to detect the presence of anti-panitumumab antibodies. Two screening immunoassays, an acid-dissociation enzyme-linked immunosorbent assay (ELISA) and a Biacore-based biosensor assay, were used to detect antibodies capable of binding to panitumumab. All samples confirmed to be positive by drug specificity in either screening immunoassay were further tested for neutralizing antibodies in a cell-based epidermal growth factor receptor (EGFR)

phosphorylation bioassay. The number of participants who developed antibodies to panitumumab is the number of participants with a non-positive (including missing) antibody result at baseline and a positive antibody result at any post-baseline time point.

This analysis includes all participants who received at least 1 dose of panitumumab and who had at least one post-baseline immunoassay result.

End point type	Secondary
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End point timeframe:

Before panitumumab administration on Day 1, Day 43, Day 169 and 30 days after last dose for all cohorts.

End point values	Age 12–17: 2.5 mg/kg QW	Age 12–17: 6 mg/kg Q2W	Age 12–17: 9 mg/kg Q3W	Age 1–11: 2.5 mg/kg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	5	4	3
Units: participants				
number (not applicable)				
Binding antibodies	1	0	0	2
Neutralizing antibodies	0	0	0	0

End point values	Age 1–11: 6 mg/kg Q2W			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: participants				
number (not applicable)				
Binding antibodies	0			
Neutralizing antibodies	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with an Objective Response

End point title	Percentage of Participants with an Objective Response
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End point description:

Disease assessments were based on investigator review of scans using modified Response Evaluation Criteria in Solid Tumors (RECIST) version 1.0 criteria. Objective response is defined as a best response of either complete response (CR) or partial response (PR). Participants with no post-baseline assessments were considered non-responders. CR or PR was confirmed no less than 4-weeks after the criteria for response were first met.

CR: Disappearance of all target and non-target lesions, normalization of tumor markers and no new lesions.

PR: At least 30% decrease in the size of target lesions, no progression of non-target lesions and no new lesions, or, the disappearance of all target lesions, persistence of 1 or more non-target lesion(s) not qualifying for either CR or progressive disease (PD) or/and maintenance of tumor marker level above normal limits and no new lesions.

Analysis includes all participants with baseline measurable disease who received at least 1 dose of panitumumab.

End point type	Secondary
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End point timeframe:

Tumor response was assessed every 8 weeks through week 48 and every 3 months thereafter until disease progression or end of study. The data cut-off for the analysis was 17 June 2015; median duration of study was 47 days.

End point values	Age 12–17: 2.5 mg/kg QW	Age 12–17: 6 mg/kg Q2W	Age 12–17: 9 mg/kg Q3W	Age 1–11: 2.5 mg/kg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	4	2
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 60.24)	0 (0 to 70.76)	0 (0 to 60.24)	0 (0 to 84.19)

End point values	Age 1–11: 6 mg/kg Q2W			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 70.76)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Disease Control

End point title	Percentage of Participants with Disease Control
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End point description:

Disease assessments were based on investigator review of scans using modified RECIST version 1.0 criteria. A participant was considered to have disease control if their best response is either a complete or partial response, or stable disease (SD). Participants without a post-baseline assessment were considered to not have disease control. A complete or partial response was confirmed no less than 4-weeks after the criteria for response were first met. A best overall response of SD requires a visit response of SD or better, no earlier than 49 days after the date of enrollment.

Stable disease: Neither sufficient shrinkage of target lesions to qualify for a PR nor sufficient increase to qualify for PD and no progression of existing non-target lesions and no new lesions.

Analysis includes all participants with baseline measurable disease who received at least 1 dose of panitumumab.

End point type	Secondary
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End point timeframe:

Tumor response was assessed every 8 weeks through week 48 and every 3 months thereafter until disease progression or end of study. The data cut-off for the analysis was 17 June 2015; median duration of study was 47 days.

End point values	Age 12–17: 2.5 mg/kg QW	Age 12–17: 6 mg/kg Q2W	Age 12–17: 9 mg/kg Q3W	Age 1–11: 2.5 mg/kg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	4	2
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 60.24)	33.33 (0.84 to 90.57)	0 (0 to 60.24)	50 (1.26 to 98.74)

End point values	Age 1–11: 6 mg/kg Q2W			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: percentage of participants				
number (confidence interval 95%)	66.67 (9.43 to 99.16)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose date to end of study date. The median duration of study is 47 days.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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Reporting groups

Reporting group title	Age 12–17: 2.5 mg/kg QW
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Reporting group description:

Participants aged 12 to 17 years received panitumumab 2.5 mg/kg administered by intravenous (IV) infusion weekly (QW) until the participant experienced disease progression, was unable to tolerate study drug, withdrew consent, or other reasons that warranted removal from the study.

Reporting group title	Age 12-17: 6 mg/kg Q2W
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Reporting group description:

Participants aged 12 to 17 years received panitumumab 6 mg/kg administered by IV infusion every 2 weeks (Q2W) until the participant experienced disease progression, was unable to tolerate study drug, withdrew consent, or other reasons that warranted removal from the study.

Reporting group title	Age 12-17: 9 mg/kg Q3W
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Reporting group description:

Participants aged 12 to 17 years received panitumumab 9 mg/kg administered by IV infusion every 3 weeks (Q3W) until the participant experienced disease progression, was unable to tolerate study drug, withdrew consent, or other reasons that warranted removal from the study.

Reporting group title	Age 1-11: 2.5 mg/kg QW
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Reporting group description:

Participants aged 1 to 11 years received panitumumab 2.5 mg/kg administered by IV infusion QW until the participant experienced disease progression, was unable to tolerate study drug, withdrew consent, or other reasons that warranted removal from the study.

Reporting group title	Age 1-11: 6 mg/kg Q2W
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Reporting group description:

Participants aged 1 to 11 years received panitumumab 6 mg/kg administered by IV infusion Q2W until the participant experienced disease progression, was unable to tolerate study drug, withdrew consent, or other reasons that warranted removal from the study.

Serious adverse events	Age 12–17: 2.5 mg/kg QW	Age 12-17: 6 mg/kg Q2W	Age 12-17: 9 mg/kg Q3W
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)	3 / 7 (42.86%)	2 / 4 (50.00%)
number of deaths (all causes)	4	0	0
number of deaths resulting from adverse events			
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
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 creatinine increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood urea increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (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
Haemoglobin decreased			
subjects affected / exposed	2 / 6 (33.33%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Osteosarcoma			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Rhabdomyosarcoma			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral haemorrhage			

subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
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	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (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
Ascites			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (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
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
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, thoracic and mediastinal disorders			
Apnoea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (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
Bronchostenosis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (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 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (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
Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (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
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (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 acidosis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory failure			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Psychiatric disorders			
Substance-induced psychotic disorder			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (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
Hydronephrosis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (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
Oliguria			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (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			
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperuricaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (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
Hypocalcaemia			

subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (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
Hypokalaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (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
Hyponatraemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (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

Serious adverse events	Age 1-11: 2.5 mg/kg QW	Age 1-11: 6 mg/kg Q2W	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 6 (50.00%)	5 / 8 (62.50%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events			
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood urea increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoglobin decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Osteosarcoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyosarcoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Apnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchostenosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 8 (25.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory acidosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Substance-induced psychotic disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hydronephrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oliguria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperuricaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Age 12-17: 2.5 mg/kg QW	Age 12-17: 6 mg/kg Q2W	Age 12-17: 9 mg/kg Q3W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)	7 / 7 (100.00%)	3 / 4 (75.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Hypotension			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
Pallor			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	2 / 4 (50.00%)
occurrences (all)	0	0	2
Chills			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	1 / 6 (16.67%)	4 / 7 (57.14%)	2 / 4 (50.00%)
occurrences (all)	1	7	2
Hypothermia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Localised oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Oedema			

subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0
Oedema peripheral subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0
Pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 7 (14.29%) 1	1 / 4 (25.00%) 1
Pyrexia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 7 (14.29%) 1	0 / 4 (0.00%) 0
Immune system disorders Cytokine release syndrome subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0
Hypersensitivity subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 7 (0.00%) 0	1 / 4 (25.00%) 1
Reproductive system and breast disorders Acquired phimosis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Aspiration subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	3 / 7 (42.86%) 4	1 / 4 (25.00%) 2
Dyspnoea subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 7 (0.00%) 0	2 / 4 (50.00%) 2
Epistaxis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	2 / 7 (28.57%) 2	2 / 4 (50.00%) 2
Nasal congestion			

subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Obstructive airways disorder			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Respiratory distress			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Rhinitis allergic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	2
Wheezing			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Agitation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Confusional state			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
Depressed mood			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0

Depression			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Disorientation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Irritability			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Blood albumin decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Blood bicarbonate decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Blood creatinine			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Blood glucose increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Haemoglobin			

subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Haemoglobin decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Heart rate increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Temperature difference of extremities			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Infusion related reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			

subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Wound secretion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Arrhythmia supraventricular			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Bradycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Sinus tachycardia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 7 (14.29%)	1 / 4 (25.00%)
occurrences (all)	1	1	1
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	2 / 4 (50.00%)
occurrences (all)	0	0	2
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 7 (28.57%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Cerebellar syndrome			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	4	0
Cognitive disorder			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Cranial nerve disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dizziness			

subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	2 / 6 (33.33%)	1 / 7 (14.29%)	1 / 4 (25.00%)
occurrences (all)	2	4	1
Hemiplegia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyperaesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Motor dysfunction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Neuropathy peripheral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nystagmus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Peripheral motor neuropathy			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Phantom pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pyramidal tract syndrome			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	2 / 4 (50.00%)
occurrences (all)	0	0	4

Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 7 (14.29%) 1	0 / 4 (0.00%) 0
Lymphopenia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	2 / 7 (28.57%) 2	1 / 4 (25.00%) 1
Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 7 (0.00%) 0	1 / 4 (25.00%) 1
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 7 (0.00%) 0	1 / 4 (25.00%) 2
Vertigo subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 7 (14.29%) 1	0 / 4 (0.00%) 0
Eye disorders Diplopia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 7 (14.29%) 2	0 / 4 (0.00%) 0
Dry eye subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 7 (14.29%) 1	0 / 4 (0.00%) 0
Erythema of eyelid subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 7 (14.29%) 1	0 / 4 (0.00%) 0
Exophthalmos subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 7 (14.29%) 1	0 / 4 (0.00%) 0
Lacrimation increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 7 (14.29%) 1	0 / 4 (0.00%) 0
Ocular hyperaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 7 (14.29%) 1	0 / 4 (0.00%) 0
Vision blurred			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 7 (14.29%) 1	0 / 4 (0.00%) 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 6 (33.33%)	1 / 7 (14.29%)	2 / 4 (50.00%)
occurrences (all)	2	1	2
Change of bowel habit			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	3 / 6 (50.00%)	3 / 7 (42.86%)	1 / 4 (25.00%)
occurrences (all)	4	3	1
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	2
Gingival bleeding			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Gingival erythema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Hypoaesthesia oral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	2
Oral pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	2

Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	4
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Decubitus ulcer			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Dermatitis acneiform			
subjects affected / exposed	2 / 6 (33.33%)	5 / 7 (71.43%)	0 / 4 (0.00%)
occurrences (all)	2	18	0
Dry skin			
subjects affected / exposed	0 / 6 (0.00%)	4 / 7 (57.14%)	2 / 4 (50.00%)
occurrences (all)	0	7	3
Erythema			
subjects affected / exposed	2 / 6 (33.33%)	2 / 7 (28.57%)	0 / 4 (0.00%)
occurrences (all)	3	2	0
Exfoliative rash			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	2 / 4 (50.00%)
occurrences (all)	0	2	3
Petechiae			
subjects affected / exposed	1 / 6 (16.67%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Pruritus			
subjects affected / exposed	2 / 6 (33.33%)	2 / 7 (28.57%)	1 / 4 (25.00%)
occurrences (all)	2	2	1
Purpura			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash			

subjects affected / exposed	2 / 6 (33.33%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	2	1	0
Rash erythematous			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Rash macular			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Rash maculo-papular			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Rash papular			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin fissures			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Skin hypopigmentation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Urinary incontinence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Urogenital haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	2 / 4 (50.00%)
occurrences (all)	0	0	2
Bone atrophy			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Flank pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Fracture pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			
subjects affected / exposed	0 / 6 (0.00%)	2 / 7 (28.57%)	0 / 4 (0.00%)
occurrences (all)	0	4	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Musculoskeletal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
Scoliosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Torticollis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Cystitis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Herpes virus infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Oral fungal infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	2
Oral herpes			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Peritonitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Purulent discharge			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash pustular			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Skin infection			

subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	2
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Streptococcal infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Alkalosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	2 / 6 (33.33%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Dehydration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hyperkalaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hypoalbuminaemia			
subjects affected / exposed	2 / 6 (33.33%)	0 / 7 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Hypocalcaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	2 / 4 (50.00%)
occurrences (all)	1	0	5

Hypoglycaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 7 (0.00%) 0	1 / 4 (25.00%) 1
Hypokalaemia subjects affected / exposed occurrences (all)	3 / 6 (50.00%) 3	0 / 7 (0.00%) 0	2 / 4 (50.00%) 3
Hypomagnesaemia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 7 (14.29%) 1	2 / 4 (50.00%) 4
Hyponatraemia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 7 (0.00%) 0	0 / 4 (0.00%) 0
Hypophosphataemia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 7 (0.00%) 0	1 / 4 (25.00%) 3

Non-serious adverse events	Age 1-11: 2.5 mg/kg QW	Age 1-11: 6 mg/kg Q2W	
Total subjects affected by non-serious adverse events subjects affected / exposed	6 / 6 (100.00%)	7 / 8 (87.50%)	
Vascular disorders			
Hypertension subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	
Hypotension subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	
Pallor subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	
General disorders and administration site conditions			
Chest pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	
Chills subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 8 (0.00%) 0	

Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	2 / 8 (25.00%)	
occurrences (all)	0	2	
Hypothermia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Localised oedema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Mucosal inflammation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Oedema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Hypersensitivity			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			

Acquired phimosis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 8 (12.50%) 1	
Respiratory, thoracic and mediastinal disorders			
Aspiration subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 8 (12.50%) 1	
Cough subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 8 (12.50%) 1	
Dyspnoea subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 8 (12.50%) 1	
Epistaxis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	
Nasal congestion subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 8 (0.00%) 0	
Obstructive airways disorder subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	
Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 8 (12.50%) 1	
Pleural effusion subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	
Respiratory distress subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	
Rhinitis allergic subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	
Wheezing			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Agitation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	2 / 8 (25.00%)	
occurrences (all)	0	2	
Confusional state			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Depressed mood			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Depression			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Disorientation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Irritability			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Blood albumin decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Blood bicarbonate decreased			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0
Blood creatinine		
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0
Blood creatinine increased		
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0
Blood glucose increased		
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1
Blood lactate dehydrogenase decreased		
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0
Blood potassium decreased		
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	2
Haemoglobin		
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0
Haemoglobin decreased		
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	2
Heart rate increased		
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0
Lymphocyte count decreased		
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	2
Neutrophil count decreased		
subjects affected / exposed	0 / 6 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	2
Platelet count decreased		
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1

Temperature difference of extremities			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
White blood cell count decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	2	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Contusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Infusion related reaction			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Skin abrasion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Wound secretion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Arrhythmia supraventricular			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Bradycardia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Sinus tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Tachycardia			

subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	2	
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Cerebellar syndrome			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Cognitive disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Cranial nerve disorder			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Headache			
subjects affected / exposed	0 / 6 (0.00%)	2 / 8 (25.00%)	
occurrences (all)	0	3	
Hemiplegia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Hyperaesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Motor dysfunction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Neuropathy peripheral			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	2	
Nystagmus			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	
occurrences (all)	1	1	

Peripheral motor neuropathy subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 8 (12.50%) 1	
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 8 (12.50%) 2	
Phantom pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	
Pyramidal tract syndrome subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	
Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	
Lymphopenia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	
Thrombocytopenia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 8 (0.00%) 0	
Ear and labyrinth disorders			
Ear pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	
Vertigo subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	
Eye disorders			
Diplopia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 8 (12.50%) 1	
Dry eye			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Erythema of eyelid			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Exophthalmos			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Lacrimation increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Ocular hyperaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Vision blurred			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Change of bowel habit			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Constipation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	3 / 8 (37.50%)	
occurrences (all)	0	3	
Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Gingival bleeding			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	

Gingival erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Hypoaesthesia oral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	3 / 8 (37.50%)	
occurrences (all)	0	4	
Oral pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Stomatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Vomiting			
subjects affected / exposed	4 / 6 (66.67%)	1 / 8 (12.50%)	
occurrences (all)	5	1	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Decubitus ulcer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Dermatitis acneiform			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Dry skin			
subjects affected / exposed	1 / 6 (16.67%)	3 / 8 (37.50%)	
occurrences (all)	1	3	
Erythema			

subjects affected / exposed	2 / 6 (33.33%)	0 / 8 (0.00%)	
occurrences (all)	4	0	
Exfoliative rash			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Petechiae			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Purpura			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	2 / 6 (33.33%)	2 / 8 (25.00%)	
occurrences (all)	2	4	
Rash erythematous			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Rash macular			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Rash maculo-papular			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Rash papular			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Skin fissures			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Skin hypopigmentation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			

Dysuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Urinary incontinence			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Urogenital haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Bone atrophy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Flank pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Fracture pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Muscular weakness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal pain			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Myalgia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Pain in extremity			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Scoliosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Torticollis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Cystitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Herpes virus infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Oral candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Oral fungal infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Oral herpes			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	

Peritonitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Purulent discharge			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Rash pustular			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Skin infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Streptococcal infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Alkalosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Decreased appetite			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Dehydration			

subjects affected / exposed	0 / 6 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	2
Hyperglycaemia		
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1
Hyperkalaemia		
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0
Hypoalbuminaemia		
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0
Hypocalcaemia		
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0
Hypoglycaemia		
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0
Hypokalaemia		
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1
Hypomagnesaemia		
subjects affected / exposed	0 / 6 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	2
Hyponatraemia		
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0
Hypophosphataemia		
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 March 2011	<ul style="list-style-type: none">- Removed the requirement for epidermal growth factor receptor (EGFR) immunohistochemical staining of tumor tissue prior to enrollment, but rather allow the central EGFR testing to be performed within 4 weeks after enrollment.- Updated the eligibility criteria to state that male subjects of reproductive potential were no longer required to use contraception precautions during the study and female subjects of childbearing potential were required to use adequate contraception precautions during treatment and for 2 months after the end of treatment.- Updated the interruption of panitumumab infusion to be consistent with the most recent guidelines regarding the management of panitumumab-related infusion reactions.- Deleted the instructions to allow treatment of subjects with central nervous system (CNS) disease only with stable glucocorticoid dosing. The dose of glucocorticoid to manage CNS disease may change while subjects are on the study.- Updated study procedures to specify that any blood and/or tumor tissue sample collected according to the Schedule of Assessments may be analyzed for any of the tests outlined in the protocol and for any tests necessary to minimize risks to study subjects. In addition, if informed consent is provided by the subject, Amgen may do additional testing on remaining samples.- Updated the Screening section to clarify that tumor tissue samples for EGFR testing should be submitted to the designated central laboratory within 4 weeks after enrollment.- Updated the End of Study Visit section to clarify that in case a subject tests positive for human antipanitumumab antibodies (HAPA) at the end of study visit, additional serum samples will be drawn and tested every 3 months from the date that the site is informed by Amgen of the positive result until the HAPA result is negative, withdrawal of consent, death, or up to 1 year after the positive result has been reported, whichever occurs first.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported