Clinical trial results:
A Phase 2 Open Label Extension Study of Conatumumab and AMG 479
Summary

EudraCT number	2010-022270-14
Trial protocol	ES
Global end of trial date	05 February 2020

Results information

Result version number	v1 (current)
This version publication date	19 February 2021
First version publication date	19 February 2021

Trial information

Trial identification

Sponsor protocol code	20101116

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01327612
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, 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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 September 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 February 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

to provide ongoing treatment with:
o conatumumab therapy, with or without co-therapy (chemotherapy with and without bevacizumab, or ganitumab) for subjects who were eligible, according to the parent study, to receive their next dose of conatumumab, or
o Ganitumab (AMG 479) therapy alone, for subjects who were eligible, according to the parent study, to receive their next dose of ganitumab.

Protection of trial subjects:

The protocol, informed consent form, other written subject information, were submitted to the Independent Ethics Committee/Institutional Review Board (IEC/IRB) for written approval. A copy of the written approval of the protocol and informed consent form must have been received by Amgen before recruitment of subjects into the study and shipment of Amgen investigational product(s).

Before a subject’s participation in the clinical study, the investigator was responsible for obtaining written informed consent from the subject or legally acceptable representative after adequate explanation of the aims, methods, anticipated benefits, and potential hazards of the study and before any protocol-specific screening procedures or any investigational products were administered.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 March 2011
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	Poland: 1
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United States: 10
Worldwide total number of subjects	12
EEA total number of subjects	2

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)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	8
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study enrolled participants with different types of solid tumors who had completed an Amgen-sponsored conatumumab or ganitumab study.
The study was conducted at 12 centers in the United States, Spain, and Poland. Results are reported by Parent study and treatment received.

Pre-assignment

Screening details:

This was an extension study that permitted participants to continue treatment with conatumumab, with or without co-therapy, or with ganitumab alone, administered at the same dose level and schedule they received at the conclusion of the parent study. Participants were treated until disease progression, intolerability, or withdrawal of consent.

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	20050118: Ganitumab 20 mg/kg

Arm description:

Ganitumab 20 mg/kg once every 4 weeks by intravenous infusion.

Arm type	Experimental
Investigational medicinal product name	Ganitumab
Investigational medicinal product code	AMG 479
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

20 mg/kg once every 4 weeks (Q4W) by intravenous infusion.

Arm title	20050171: Conatumumab 0.45 mg/kg

Arm description:

Conatumumab 0.45 mg/kg every 2 weeks by intravenous infusion.

Arm type	Experimental
Investigational medicinal product name	Conatumumab
Investigational medicinal product code	AMG 655
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

0.45 mg/kg once every 2 weeks (Q2W) by intravenous infusion.

Arm title	20060295: Conatumumab 3 mg/kg

Arm description:

Conatumumab 3 mg/kg every 3 weeks by intravenous infusion.

Arm type	Experimental

Investigational medicinal product name	Conatumumab
Investigational medicinal product code	AMG 655
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

3 mg/kg once every 3 weeks (Q3W) by intravenous infusion.

Arm title	20060340: Conatumumab 5 mg/kg

Arm description:

Conatumumab 5 mg/kg once every 3 weeks by intravenous infusion.

Arm type	Experimental
Investigational medicinal product name	Conatumumab
Investigational medicinal product code	AMG 655
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

5 mg/kg once every 3 weeks (Q3W) by intravenous infusion.

Arm title	20060464: Conatumumab 2 mg/kg + mFOLFOX6 + Bevacizumab

Arm description:

Conatumumab 2 mg/kg once every 2 weeks by intravenous infusion in addition to modified FOLFOX6 chemotherapy and bevacizumab 5 mg/kg once every 2 weeks.

Arm type	Experimental
Investigational medicinal product name	Conatumumab
Investigational medicinal product code	AMG 655
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

2 mg/kg once every 2 weeks (Q2W) by intravenous infusion.

Arm title	20060464: Conatumumab 10 mg/kg + mFOLFOX6 ± Bevacizumab

Arm description:

Conatumumab 10 mg/kg once every 2 weeks by intravenous infusion in addition to modified FOLFOX6 (mFOLFOX6) chemotherapy, with or without bevacizumab 5 mg/kg once every 2 weeks.

Arm type	Experimental
Investigational medicinal product name	Conatumumab
Investigational medicinal product code	AMG 655
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

10 mg/kg once every 2 weeks (Q2W) by intravenous infusion.

Arm title	20070411: Conatumumab 15 mg/kg + Ganitumab 18 mg/kg

Arm description:

Conatumumab 15 mg/kg + ganitumab 18 mg/kg once every 3 weeks by intravenous infusion.

Arm type	Experimental

Investigational medicinal product name	Conatumumab
Investigational medicinal product code	AMG 655
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

15 mg/kg once every 3 weeks (Q3W) by intravenous infusion.

Investigational medicinal product name	Ganitumab
Investigational medicinal product code	AMG 479
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

18 mg/kg once every 3 weeks (Q3W) by intravenous infusion.

Number of subjects in period 1	20050118: Ganitumab 20 mg/kg	20050171: Conatumumab 0.45 mg/kg	20060295: Conatumumab 3 mg/kg
Started	2	1	1
Completed	1	0	0
Not completed	1	1	1
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	-	-	-
Administrative Decision	-	-	-
Disease Progression	1	1	1

Number of subjects in period 1	20060340: Conatumumab 5 mg/kg	20060464: Conatumumab 2 mg/kg + mFOLFOX6 + Bevacizumab	20060464: Conatumumab 10 mg/kg + mFOLFOX6 ± Bevacizumab
Started	1	2	3
Completed	0	0	0
Not completed	1	2	3
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	-	-	1
Administrative Decision	1	-	-
Disease Progression	-	1	2

Number of subjects in period 1	20070411: Conatumumab 15 mg/kg + Ganitumab 18 mg/kg
Started	2
Completed	0
Not completed	2
Adverse event, serious fatal	-
Consent withdrawn by subject	-

Administrative Decision	-
Disease Progression	2

Baseline characteristics

Reporting groups	
Reporting group title	20050118: Ganitumab 20 mg/kg
Reporting group description:	
Ganitumab 20 mg/kg once every 4 weeks by intravenous infusion.	
Reporting group title	20050171: Conatumumab 0.45 mg/kg
Reporting group description:	
Conatumumab 0.45 mg/kg every 2 weeks by intravenous infusion.	
Reporting group title	20060295: Conatumumab 3 mg/kg
Reporting group description:	
Conatumumab 3 mg/kg every 3 weeks by intravenous infusion.	
Reporting group title	20060340: Conatumumab 5 mg/kg
Reporting group description:	
Conatumumab 5 mg/kg once every 3 weeks by intravenous infusion.	
Reporting group title	20060464: Conatumumab 2 mg/kg + mFOLFOX6 + Bevacizumab
Reporting group description:	
Conatumumab 2 mg/kg once every 2 weeks by intravenous infusion in addition to modified FOLFOX6 chemotherapy and bevacizumab 5 mg/kg once every 2 weeks.	
Reporting group title	20060464: Conatumumab 10 mg/kg + mFOLFOX6 ± Bevacizumab
Reporting group description:	
Conatumumab 10 mg/kg once every 2 weeks by intravenous infusion in addition to modified FOLFOX6 (mFOLFOX6) chemotherapy, with or without bevacizumab 5 mg/kg once every 2 weeks.	
Reporting group title	20070411: Conatumumab 15 mg/kg + Ganitumab 18 mg/kg
Reporting group description:	
Conatumumab 15 mg/kg + ganitumab 18 mg/kg once every 3 weeks by intravenous infusion.	

Reporting group values	20050118: Ganitumab 20 mg/kg	20050171: Conatumumab 0.45 mg/kg	20060295: Conatumumab 3 mg/kg
Number of subjects	2	1	1
Age Categorical Units: participants			
18 - 64 years	1	1	1
65 - 74 years	1	0	0
75 - 84 years	0	0	0
≥ 85 years	0	0	0
Age Continuous Units: years			
median	60.0	57.0	44.0
full range (min-max)	50.0 to 70.0	57.0 to 57.0	44.0 to 44.0
Sex: Female, Male Units: participants			
Female	1	0	1
Male	1	1	0
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0

Black or African American	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
White	2	1	1
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	2	1	1

Reporting group values	20060340: Conatumumab 5 mg/kg	20060464: Conatumumab 2 mg/kg + mFOLFOX6 + Bevacizumab	20060464: Conatumumab 10 mg/kg + mFOLFOX6 ± Bevacizumab
Number of subjects	1	2	3
Age Categorical Units: participants			
18 - 64 years	1	1	2
65 - 74 years	0	1	1
75 - 84 years	0	0	0
≥ 85 years	0	0	0
Age Continuous Units: years			
median	46.0	66.5	54.0
full range (min-max)	46.0 to 46.0	61.0 to 72.0	49.0 to 66.0
Sex: Female, Male Units: participants			
Female	0	1	1
Male	1	1	2
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	1
Black or African American	0	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
White	1	2	1
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	1	2	3

Reporting group values	20070411: Conatumumab 15 mg/kg + Ganitumab 18 mg/kg	Total	
Number of subjects	2	12	
Age Categorical Units: participants			
18 - 64 years	1	8	
65 - 74 years	0	3	
75 - 84 years	1	1	
≥ 85 years	0	0	

Age Continuous Units: years			
median	68.0		
full range (min-max)	57.0 to 79.0	-	
Sex: Female, Male Units: participants			
Female	1	5	
Male	1	7	
Race Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	1	
Black or African American	0	1	
Native Hawaiian or Other Pacific Islander	0	0	
White	2	10	
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	2	12	

End points

End points reporting groups

Reporting group title	20050118: Ganitumab 20 mg/kg
Reporting group description:	
Ganitumab 20 mg/kg once every 4 weeks by intravenous infusion.	
Reporting group title	20050171: Conatumumab 0.45 mg/kg
Reporting group description:	
Conatumumab 0.45 mg/kg every 2 weeks by intravenous infusion.	
Reporting group title	20060295: Conatumumab 3 mg/kg
Reporting group description:	
Conatumumab 3 mg/kg every 3 weeks by intravenous infusion.	
Reporting group title	20060340: Conatumumab 5 mg/kg
Reporting group description:	
Conatumumab 5 mg/kg once every 3 weeks by intravenous infusion.	
Reporting group title	20060464: Conatumumab 2 mg/kg + mFOLFOX6 + Bevacizumab
Reporting group description:	
Conatumumab 2 mg/kg once every 2 weeks by intravenous infusion in addition to modified FOLFOX6 chemotherapy and bevacizumab 5 mg/kg once every 2 weeks.	
Reporting group title	20060464: Conatumumab 10 mg/kg + mFOLFOX6 ± Bevacizumab
Reporting group description:	
Conatumumab 10 mg/kg once every 2 weeks by intravenous infusion in addition to modified FOLFOX6 (mFOLFOX6) chemotherapy, with or without bevacizumab 5 mg/kg once every 2 weeks.	
Reporting group title	20070411: Conatumumab 15 mg/kg + Ganitumab 18 mg/kg
Reporting group description:	
Conatumumab 15 mg/kg + ganitumab 18 mg/kg once every 3 weeks by intravenous infusion.	

Primary: Number of Participants with Adverse Events

End point title	Number of Participants with Adverse Events[1]
End point description:	
An adverse event is defined as any untoward medical occurrence in a clinical trial participant, including worsening of a pre-existing medical condition. The event does not necessarily have a causal relationship with study treatment.	
End point type	Primary
End point timeframe:	
From first dose of study drug in the extension study to 30 days after last dose; median duration of treatment with conatumumab was 1190.5 days and 1163.0 days for ganitumab.	

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 analyses were planned or conducted.

End point values	20050118: Ganitumab 20 mg/kg	20050171: Conatumumab 0.45 mg/kg	20060295: Conatumumab 3 mg/kg	20060340: Conatumumab 5 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	1	1	1
Units: participants	2	1	1	1

End point values	20060464: Conatumumab 2 mg/kg + mFOLFOX6 + Bevacizumab	20060464: Conatumumab 10 mg/kg + mFOLFOX6 ± Bevacizumab	20070411: Conatumumab 15 mg/kg + Ganitumab 18 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	3	2	
Units: participants	2	3	2	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Serious Adverse Events

End point title	Number of Participants with Serious Adverse Events[2]

End point description:

A serious adverse event is defined as an adverse event that met at least 1 of the following serious criteria:
- fatal,
- life threatening (places the participant at immediate risk of death),
- required in-patient hospitalization or prolongation of existing hospitalization,
- resulted in persistent or significant disability/incapacity,
- congenital anomaly/birth defect, and/or
- other medically important serious event.

End point type	Primary

End point timeframe:

From first dose of study drug in the extension study to 30 days after last dose; median duration of treatment with conatumumab was 1190.5 days and 1163.0 days for ganitumab.

Notes:

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

End point values	20050118: Ganitumab 20 mg/kg	20050171: Conatumumab 0.45 mg/kg	20060295: Conatumumab 3 mg/kg	20060340: Conatumumab 5 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	1	1	1
Units: participants	1	0	1	0

End point values	20060464: Conatumumab 2 mg/kg + mFOLFOX6 + Bevacizumab	20060464: Conatumumab 10 mg/kg + mFOLFOX6 ± Bevacizumab	20070411: Conatumumab 15 mg/kg + Ganitumab 18 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	3	2	
Units: participants	1	3	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Change from Baseline in Blood Pressure

End point title	Maximum Change from Baseline in Blood Pressure

End point description:

Maximum change from baseline is defined for each participant as the maximum change from baseline value observed across all visits.

End point type	Secondary

End point timeframe:

Baseline and day 1 of each treatment cycle (every 2, 3, or 4 weeks depending on dosing schedule) up to 30 days after last dose; median duration of treatment with conatumumab was 1190.5 days and 1163.0 days for ganitumab.

End point values	20050118: Ganitumab 20 mg/kg	20050171: Conatumumab 0.45 mg/kg	20060295: Conatumumab 3 mg/kg	20060340: Conatumumab 5 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	1	1	1
Units: mmHg				
median (full range (min-max))				
Systolic blood pressure	5.5 (-1 to 12)	7.0 (7 to 7)	54.0 (54 to 54)	37.0 (37 to 37)
Diastolic blood pressure	7.5 (1 to 14)	1.0 (1 to 1)	10.0 (10 to 10)	13.0 (13 to 13)

End point values	20060464: Conatumumab 2 mg/kg + mFOLFOX6 + Bevacizumab	20060464: Conatumumab 10 mg/kg + mFOLFOX6 ± Bevacizumab	20070411: Conatumumab 15 mg/kg + Ganitumab 18 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	3	2	
Units: mmHg				
median (full range (min-max))				
Systolic blood pressure	42.0 (42 to 42)	16.0 (16 to 46)	32.5 (10 to 55)	
Diastolic blood pressure	27.5 (21 to 34)	12.0 (10 to 22)	23.5 (19 to 28)	

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Change from Baseline in Blood Pressure

End point title	Minimum Change from Baseline in Blood Pressure

End point description:

Minimum change from baseline is defined for each participant as the minimum change from baseline value observed across all visits.

End point type	Secondary

End point timeframe:

Baseline and day 1 of each treatment cycle (every 2, 3, or 4 weeks depending on dosing schedule) up to 30 days after last dose; median duration of treatment with conatumumab was 1190.5 days and 1163.0 days for ganitumab.

End point values	20050118: Ganitumab 20 mg/kg	20050171: Conatumumab 0.45 mg/kg	20060295: Conatumumab 3 mg/kg	20060340: Conatumumab 5 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	1	1	1
Units: mmHg				
median (full range (min-max))				
Systolic blood pressure	-28.5 (-41 to -16)	-45.0 (-45 to -45)	-20.0 (-20 to -20)	-21.0 (-21 to -21)
Diastolic blood pressure	-19.5 (-26 to -13)	-27.0 (-27 to -27)	-20.0 (-20 to -20)	-25.0 (-25 to -25)

End point values	20060464: Conatumumab 2 mg/kg + mFOLFOX6 + Bevacizumab	20060464: Conatumumab 10 mg/kg + mFOLFOX6 ± Bevacizumab	20070411: Conatumumab 15 mg/kg + Ganitumab 18 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	3	2	
Units: mmHg				
median (full range (min-max))				
Systolic blood pressure	-22.5 (-34 to -11)	-32.0 (-38 to -17)	-12.0 (-21 to -3)	
Diastolic blood pressure	-8.5 (-14 to -3)	-17.0 (-18 to -8)	-10.0 (-13 to -7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with CTCAE Grade 3 or Higher Clinical Laboratory Toxicities

End point title	Number of Participants with CTCAE Grade 3 or Higher Clinical Laboratory Toxicities

End point description:

Laboratory toxicities were graded according to the Common Terminology Criteria for Adverse Events (CTCAE) version 3.0.

End point type	Secondary

End point timeframe:

From first dose of study drug in the extension study to 30 days after last dose; median duration of treatment with conatumumab was 1190.5 days and 1163.0 days for ganitumab.

End point values	20050118: Ganitumab 20 mg/kg	20050171: Conatumumab 0.45 mg/kg	20060295: Conatumumab 3 mg/kg	20060340: Conatumumab 5 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	1	1	1
Units: participants	0	0	1	0

End point values	20060464: Conatumumab 2 mg/kg + mFOLFOX6 + Bevacizumab	20060464: Conatumumab 10 mg/kg + mFOLFOX6 ± Bevacizumab	20070411: Conatumumab 15 mg/kg + Ganitumab 18 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	3	2	
Units: participants	2	2	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Best Overall Response

End point title	Best Overall Response

End point description:

Radiological assessments to evaluate disease extent (with change compared to nadir from the parent protocol) were performed at regular intervals, at a minimum once every 6 months or more frequently if clinically indicated (starting from their last scan on the parent protocol), per standard of care (SOC) at each facility. Tumor response was assessed by the Investigator as either complete response, partial response, stable disease, or progressive disease.

End point type	Secondary

End point timeframe:

Approximately every 6 months until end of treatment; median duration of treatment with conatumumab was 1190.5 days and 1163.0 days for ganitumab.

End point values	20050118: Ganitumab 20 mg/kg	20050171: Conatumumab 0.45 mg/kg	20060295: Conatumumab 3 mg/kg	20060340: Conatumumab 5 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	1	1	1
Units: participants				
Complete response	0	1	0	1
Partial response	0	0	0	0
Stable disease	2	0	1	0
Progressive disease	0	0	0	0

End point values	20060464: Conatumumab 2 mg/kg + mFOLFOX6 + Bevacizumab	20060464: Conatumumab 10 mg/kg + mFOLFOX6 ± Bevacizumab	20070411: Conatumumab 15 mg/kg + Ganitumab 18 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	3	2	
Units: participants				
Complete response	1	0	0	
Partial response	1	1	1	
Stable disease	0	2	1	
Progressive disease	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Disease Progressions and Death Due to Disease Progression

End point title	Number of Participants with Disease Progressions and Death Due to Disease Progression

End point description:

End point type	Secondary

End point timeframe:

From first dose of study drug in the extension study to 30 days after last dose; median duration of treatment with conatumumab was 1190.5 days and 1163.0 days for ganitumab.

End point values	20050118: Ganitumab 20 mg/kg	20050171: Conatumumab 0.45 mg/kg	20060295: Conatumumab 3 mg/kg	20060340: Conatumumab 5 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	1	1	1
Units: participants				
Disease progression	1	1	1	0
Death due to disease progression	0	0	0	0

End point values	20060464: Conatumumab 2 mg/kg + mFOLFOX6 + Bevacizumab	20060464: Conatumumab 10 mg/kg + mFOLFOX6 ± Bevacizumab	20070411: Conatumumab 15 mg/kg + Ganitumab 18 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	3	2	
Units: participants				
Disease progression	2	2	2	
Death due to disease progression	1	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug in the extension study to 30 days after last dose; median duration of treatment with conatumumab was 1190.5 days and 1163.0 days for ganitumab.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	20050118: Ganitumab 20 mg/kg

Reporting group description:

Ganitumab 20 mg/kg once every 4 weeks by intravenous infusion.

Reporting group title	20050171: Conatumumab 0.45 mg/kg

Reporting group description:

Conatumumab 0.45 mg/kg every 2 weeks by intravenous infusion.

Reporting group title	20060295: Conatumumab 3 mg/kg

Reporting group description:

Conatumumab 3 mg/kg every 3 weeks by intravenous infusion.

Reporting group title	20060340: Conatumumab 5 mg/kg

Reporting group description:

Conatumumab 5 mg/kg once every 3 weeks by intravenous infusion.

Reporting group title	20060464: Conatumumab 2 mg/kg + mFOLFOX6 + Bevacizumab

Reporting group description:

Conatumumab 2 mg/kg once every 2 weeks by intravenous infusion in addition to modified FOLFOX6 chemotherapy and bevacizumab 5 mg/kg once every 2 weeks.

Reporting group title	20060464: Conatumumab 10 mg/kg + mFOLFOX6 ± Bevacizumab

Reporting group description:

Conatumumab 10 mg/kg once every 2 weeks by intravenous infusion in addition to modified FOLFOX6 chemotherapy, with or without bevacizumab 5 mg/kg once every 2 weeks.

Reporting group title	20070411: Conatumumab 15 mg/kg + Ganitumab 18 mg/kg

Reporting group description:

Conatumumab 15 mg/kg + ganitumab 18 mg/kg once every 3 weeks by intravenous infusion.

Serious adverse events	20050118: Ganitumab 20 mg/kg	20050171: Conatumumab 0.45 mg/kg	20060295: Conatumumab 3 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)	0 / 1 (0.00%)	1 / 1 (100.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Rectal cancer metastatic			

subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
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			
Hip fracture			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
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			
Myocardial infarction			
subjects affected / exposed	1 / 2 (50.00%)	0 / 1 (0.00%)	0 / 1 (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
Surgical and medical procedures			
Transurethral bladder resection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
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 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticular perforation			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
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 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			

subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
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 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
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			
Dyspnoea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
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			
Renal failure			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
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			
Lumbar spinal stenosis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
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			
Abdominal wall abscess			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
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 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis C			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	1 / 1 (100.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
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			
Hyponatraemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
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	20060340: Conatumumab 5 mg/kg	20060464: Conatumumab 2 mg/kg + mFOLFOX6 + Bevacizumab	20060464: Conatumumab 10 mg/kg + mFOLFOX6 ± Bevacizumab
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	3 / 3 (100.00%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Rectal cancer metastatic			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	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 / 1	0 / 0
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (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			

Myocardial infarction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (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			
Transurethral bladder resection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (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 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticular perforation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	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
Haemoptysis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (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			
Renal failure			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (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
Musculoskeletal and connective tissue disorders			
Lumbar spinal stenosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (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
Infections and infestations			
Abdominal wall abscess			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (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
Gastroenteritis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (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
Hepatitis C			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (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 / 1 (0.00%)	1 / 2 (50.00%)	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

Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	20070411: Conatumumab 15 mg/kg + Ganitumab 18 mg/kg		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Rectal cancer metastatic			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Transurethral bladder resection			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	0 / 2 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diverticular perforation				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemoptysis				
subjects affected / exposed	1 / 2 (50.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Renal failure				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Musculoskeletal and connective tissue disorders			
Lumbar spinal stenosis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Abdominal wall abscess			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatitis C			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	20050118: Ganitumab 20 mg/kg	20050171: Conatumumab 0.45 mg/kg	20060295: Conatumumab 3 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	1 / 1 (100.00%)	1 / 1 (100.00%)

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Lipoma			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Oesophageal carcinoma			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Transitional cell carcinoma			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
May-Thurner syndrome			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Peripheral venous disease			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			

Micrographic skin surgery			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin neoplasm excision			
subjects affected / exposed	0 / 2 (0.00%)	1 / 1 (100.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Tooth extraction			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Catheter site pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
General physical health deterioration			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Injection site bruising			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			

subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 2 (50.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Swelling			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 2 (50.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Temperature intolerance			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Genital rash			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nipple pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Prostatomegaly			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vaginal odour			

subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal pruritus			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Allergic bronchitis			
subjects affected / exposed	1 / 2 (50.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	0 / 2 (0.00%)	1 / 1 (100.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Dry throat			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Lung infiltration			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			

subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pleuritic pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pulmonary congestion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Libido decreased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Product issues			
Device occlusion			

subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Investigations			
Amylase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Anticoagulation drug level above therapeutic			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood magnesium increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood testosterone decreased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood uric acid increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Chest X-ray abnormal			

subjects affected / exposed	0 / 2 (0.00%)	1 / 1 (100.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
International normalised ratio increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	2
White blood cell count increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
White blood cells urine			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Eye contusion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Eyelid injury			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Fibula fracture			
subjects affected / exposed	1 / 2 (50.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Humerus fracture			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Tooth fracture			

subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Wound complication			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Cardiac flutter			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Cardiomegaly			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 2 (50.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	1 / 2 (50.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	1 / 2 (50.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Seizure			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Syncope			

subjects affected / exposed	1 / 2 (50.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Tremor			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Splenomegaly			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Periorbital oedema			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 2 (50.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			

subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Lip pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Lip swelling			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Loose tooth			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Tooth loss			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Toothache			

subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 2 (0.00%)	1 / 1 (100.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Rash macular			
subjects affected / exposed	1 / 2 (50.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Skin hypopigmentation			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin lesion			

subjects affected / exposed	0 / 2 (0.00%)	1 / 1 (100.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nocturia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 2 (50.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	1 / 2 (50.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Bone pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Intervertebral disc degeneration			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Joint effusion			
subjects affected / exposed	1 / 2 (50.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Muscular weakness			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			

subjects affected / exposed	1 / 2 (50.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 1 (100.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	1 / 2 (50.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Abdominal infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Abdominal wall abscess			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Anal abscess			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Eyelid infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Furuncle			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hepatitis C			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	2

Herpes zoster			
subjects affected / exposed	0 / 2 (0.00%)	1 / 1 (100.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Peritonitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	1 / 2 (50.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Postoperative wound infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	1 / 2 (50.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Tooth infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 2 (50.00%)	1 / 1 (100.00%)	0 / 1 (0.00%)
occurrences (all)	1	2	0
Urinary tract infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vaginal infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dehydration			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dyslipidaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hyperlipidaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			

subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	20060340: Conatumumab 5 mg/kg	20060464: Conatumumab 2 mg/kg + mFOLFOX6 + Bevacizumab	20060464: Conatumumab 10 mg/kg + mFOLFOX6 ± Bevacizumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	2 / 2 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lipoma			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Oesophageal carcinoma			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Transitional cell carcinoma			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hot flush			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hypertension			
subjects affected / exposed	1 / 1 (100.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	2	1	0

Hypotension			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	4
May-Thurner syndrome			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Peripheral venous disease			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Surgical and medical procedures			
Micrographic skin surgery			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Skin neoplasm excision			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tooth extraction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	2
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Catheter site pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Chills			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Fatigue			
subjects affected / exposed	1 / 1 (100.00%)	2 / 2 (100.00%)	2 / 3 (66.67%)
occurrences (all)	1	6	9
Gait disturbance			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
General physical health deterioration			

subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Injection site bruising			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	3
Peripheral swelling			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Pyrexia			
subjects affected / exposed	0 / 1 (0.00%)	2 / 2 (100.00%)	2 / 3 (66.67%)
occurrences (all)	0	3	3
Swelling			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Temperature intolerance			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	6	0
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Genital rash			

subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Nipple pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Prostatomegaly			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Vaginal odour			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Vulvovaginal pruritus			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Respiratory, thoracic and mediastinal disorders			
Allergic bronchitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dry throat			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dysphonia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Epistaxis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	1 / 3 (33.33%)
occurrences (all)	0	1	2
Hypoxia			

subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Lung infiltration			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Pleural effusion			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pleuritic pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Productive cough			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pulmonary congestion			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pulmonary embolism			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	2 / 3 (66.67%)
occurrences (all)	0	1	2
Sleep apnoea syndrome			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Wheezing			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Depression			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Libido decreased			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Product issues			
Device occlusion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
Amylase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	2
Anticoagulation drug level above therapeutic			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	2 / 3 (66.67%)
occurrences (all)	1	0	5
Blood magnesium increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Blood phosphorus increased			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Blood testosterone decreased			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood urea increased			

subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood uric acid increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Chest X-ray abnormal			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	3
White blood cell count increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
White blood cells urine			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Eye contusion			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Eyelid injury			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Fibula fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Humerus fracture			

subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Tooth fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Wound complication			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Cardiac disorders			
Cardiac flutter			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Cardiomegaly			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Headache			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Neuropathy peripheral			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Paraesthesia			

subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Seizure			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	19
Leukopenia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Lymphopenia			
subjects affected / exposed	1 / 1 (100.00%)	1 / 2 (50.00%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Neutropenia			
subjects affected / exposed	0 / 1 (0.00%)	2 / 2 (100.00%)	0 / 3 (0.00%)
occurrences (all)	0	46	0
Splenomegaly			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Thrombocytopenia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	22	0
Eye disorders			
Periorbital oedema			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	5
Abdominal pain lower			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	0 / 1 (0.00%)	2 / 2 (100.00%)	1 / 3 (33.33%)
occurrences (all)	0	8	6
Dry mouth			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dysphagia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Haematochezia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Lip pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Lip swelling			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Loose tooth			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	9
Oral pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	1 / 3 (33.33%)
occurrences (all)	0	1	1

Stomatitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Tooth loss			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	1 / 3 (33.33%)
occurrences (all)	0	1	3
Vomiting			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	10
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dry skin			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	4
Eczema			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Pruritus			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Rash macular			

subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin hypopigmentation			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Skin lesion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Nocturia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	1 / 1 (100.00%)	1 / 2 (50.00%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Bone pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Flank pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Groin pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Intervertebral disc degeneration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Joint effusion			

subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	3
Musculoskeletal pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	3
Pain in extremity			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	1 / 3 (33.33%)
occurrences (all)	0	1	5
Infections and infestations			
Abdominal infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Abdominal wall abscess			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Anal abscess			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Cellulitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Cystitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Eyelid infection			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Furuncle			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hepatitis C			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Peritonitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Postoperative wound infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Tooth infection			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 1 (100.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Urinary tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	9
Vaginal infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2

Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	2 / 3 (66.67%)
occurrences (all)	0	1	2
Dehydration			
subjects affected / exposed	1 / 1 (100.00%)	1 / 2 (50.00%)	2 / 3 (66.67%)
occurrences (all)	1	1	7
Dyslipidaemia			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hyperglycaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperlipidaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hyperuricaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hypoalbuminaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Hypocalcaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			

subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	1 / 3 (33.33%)
occurrences (all)	0	1	9
Hypomagnesaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	4
Hyponatraemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	4	0	1

Non-serious adverse events	20070411: Conatumumab 15 mg/kg + Ganitumab 18 mg/kg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Lipoma			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Oesophageal carcinoma			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Transitional cell carcinoma			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		

Hot flush			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
May-Thurner syndrome			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Peripheral venous disease			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Surgical and medical procedures			
Micrographic skin surgery			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Skin neoplasm excision			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Tooth extraction			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	2		
Catheter site pain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Fatigue			

subjects affected / exposed	1 / 2 (50.00%)			
occurrences (all)	1			
Gait disturbance				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
General physical health deterioration				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
Injection site bruising				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
Malaise				
subjects affected / exposed	1 / 2 (50.00%)			
occurrences (all)	1			
Mucosal inflammation				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
Oedema peripheral				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
Peripheral swelling				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
Pyrexia				
subjects affected / exposed	1 / 2 (50.00%)			
occurrences (all)	1			
Swelling				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
Systemic inflammatory response syndrome				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
Temperature intolerance				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			

Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Genital rash			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Nipple pain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Prostatomegaly			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Vaginal odour			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Vulvovaginal pruritus			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Allergic bronchitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Dry throat			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Dysphonia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Epistaxis			

subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Hypoxia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Lung infiltration			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Pleural effusion			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Pleuritic pain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Productive cough			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Pulmonary congestion			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Pulmonary embolism			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Sleep apnoea syndrome			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Wheezing			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		

Confusional state			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Libido decreased			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Product issues			
Device occlusion			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Investigations			
Amylase increased			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Anticoagulation drug level above therapeutic			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Blood creatinine increased			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Blood magnesium increased			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Blood phosphorus increased			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Blood testosterone decreased			

subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Blood urea increased			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Blood uric acid increased			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Chest X-ray abnormal			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Hepatic enzyme increased			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
International normalised ratio increased			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
White blood cell count increased			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
White blood cells urine			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Eye contusion			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Eyelid injury			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Fibula fracture			

subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Humerus fracture			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Ligament sprain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Tooth fracture			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Wound complication			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Cardiac flutter			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Cardiomegaly			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Tachycardia			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	2		
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Hypoaesthesia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Neuropathy peripheral			

subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Paraesthesia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Seizure			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Syncope			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Tremor			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Leukopenia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Lymphopenia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Neutropenia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Splenomegaly			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Thrombocytopenia			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Eye disorders			
Periorbital oedema			

subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Abdominal pain lower			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Dry mouth			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Dysphagia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Haematochezia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Lip pain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Lip swelling			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Loose tooth			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		

Oral pain subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Stomatitis subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Tooth loss subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Toothache subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Vomiting subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Hepatobiliary disorders Hyperbilirubinaemia subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1		
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Dry skin subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Eczema subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Palmar-plantar erythrodysaesthesia syndrome subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Pruritus subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Rash			

subjects affected / exposed occurrences (all) Rash macular subjects affected / exposed occurrences (all) Skin hypopigmentation subjects affected / exposed occurrences (all) Skin lesion subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 1 / 2 (50.00%) 2		
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all) Nocturia subjects affected / exposed occurrences (all)	 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Bone pain subjects affected / exposed occurrences (all) Flank pain subjects affected / exposed occurrences (all) Groin pain subjects affected / exposed occurrences (all) Intervertebral disc degeneration	 2 / 2 (100.00%) 2 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0		

subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Joint effusion			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Muscular weakness			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Abdominal infection			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Abdominal wall abscess			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Anal abscess			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Cellulitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Conjunctivitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Cystitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		

Eyelid infection				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
Furuncle				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
Hepatitis C				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
Herpes zoster				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
Nasopharyngitis				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
Peritonitis				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
Pneumonia				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
Postoperative wound infection				
subjects affected / exposed	1 / 2 (50.00%)			
occurrences (all)	1			
Sinusitis				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
Tooth infection				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
Upper respiratory tract infection				
subjects affected / exposed	1 / 2 (50.00%)			
occurrences (all)	6			
Urinary tract infection				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			

Vaginal infection			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	2		
Dehydration			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	2		
Dyslipidaemia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Hypercholesterolaemia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	10		
Hyperkalaemia			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	2		
Hyperlipidaemia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Hyperuricaemia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Hypoalbuminaemia			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	2		
Hypocalcaemia			

subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Hypomagnesaemia			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	2		
Hyponatraemia			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	5		
Hypophosphataemia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 November 2013	The protocol was amended primarily to change the interval of tumor scans from 3 to 6 months (±1 months or more frequently if clinically indicated) in order to reduce the risk to subjects due to potential cumulative radiation exposure given that all subjects have been on study treatment for 3.5 to 7 years since the initial dose on the Parent Study and continue to do well either responding to treatment or are clinically stable. In the addition, the following changes have been incorporated into the protocol: - Update the sponsor contact information. - Remove the description of the formulation of the conatumumab and AMG 479 investigational product materials from the protocol since the information is already provided to the investigator in the Investigational Product Instruction Manual. - Allow the investigator to use previous cycle's amylase and lipase results, if present cycle's results are not available before dosing - Revision of the reporting language of SAE's within the Treatment period and Day 30 Safety Follow Up Visit - Update reasons for removal from protocol-specified product(s) or observation in accordance with reasons available on the end of study case report form. - Update Reporting Procedures for SAE to inform the investigator to report SAEs that occurs outside the protocol-specified reporting period per the Guidance CT-3. - Update EAC data capture instructions in Study Monitoring and Data Collection to align with the current standard instructions in the Amgen protocol template. - Add Investigator Responsibilities for Data Collection per the latest version of the Amgen protocol template - Update Publication Policy to only reference the International Committee Medical Journal Editors (ICMJE) guidelines without specifying a version or set of criteria. - Other administrative corrections were made throughout the protocol.
11 April 2017	• To describe the two-step transition to NantCell in manufacturing, labeling, and distribution of AMG 479. • To update the Key Sponsor Contacts • To update Section 9.3, Pregnancy and Lactation Reporting • To update Appendix C, Sample Serious Adverse Event Form, Appendix D, Pregnancy Notification Worksheet, and Appendix E, Lactation Notification Worksheet

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported