Clinical trial results:
A Single Arm, Open Label Multicentre Extension Study of Bevacizumab in Patients With Solid Tumours on Study Treatment With Bevacizumab, at the End of A F. Hoffmann-La Roche and/or Genentech Sponsored Study

Summary

EudraCT number	2011-002009-31
Trial protocol	CZ GB ES SK NL FR IT DE EE HU LV AT GR BG
Global end of trial date	27 September 2019

Results information

Result version number	v1 (current)
This version publication date	27 September 2020
First version publication date	27 September 2020

Trial information

Trial identification

Sponsor protocol code	MO25757

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01588184
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.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	27 March 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 September 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To provide continued bevacizumab therapy as single agent or in combination with an anti-cancer drug to patients with cancer, who were previously enrolled in a F. Hoffmann-La Roche (Roche)/ Genentech sponsored bevacizumab study (i.e. the Parent, P-trial) and who derived benefit from the therapy administered

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 July 2012
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	Austria: 1
Country: Number of subjects enrolled	Brazil: 8
Country: Number of subjects enrolled	Bulgaria: 1
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Czech Republic: 2
Country: Number of subjects enrolled	Estonia: 1
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	Italy: 13
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 3
Country: Number of subjects enrolled	Mexico: 9
Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	Romania: 5
Country: Number of subjects enrolled	Russian Federation: 14
Country: Number of subjects enrolled	Slovakia: 1
Country: Number of subjects enrolled	South Africa: 1
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	Turkey: 1

Country: Number of subjects enrolled	United Kingdom: 3
Worldwide total number of subjects	95
EEA total number of subjects	56

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)	68
From 65 to 84 years	27
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The number of participants enrolled over the planned recruitment period was open. 95 participants actually enrolled in this study.

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	Breast Cancer

Arm description:

Participants will receive bevacizumab until progression of disease or unacceptable toxicity, withdrawal of consent or death whichever occurs first.

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

Dosage and administration details:

Bevacizumab will be administered at 7.5 or 15 milligrams per kilogram (mg/kg) intravenously every 3 weeks (Q3W), or 5 or 10 mg/kg intravenously every 2 weeks (Q2W).

Arm title	Ovarian Cancer or Peritoneal Carcinoma

Arm description:

Participants will receive bevacizumab until progression of disease or unacceptable toxicity, withdrawal of consent or death whichever occurs first.

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

Dosage and administration details:

Bevacizumab will be administered at 7.5 or 15 milligrams per kilogram (mg/kg) intravenously every 3 weeks (Q3W), or 5 or 10 mg/kg intravenously every 2 weeks (Q2W).

Arm title	Colorectal Cancer

Arm description:

Participants will receive bevacizumab until progression of disease or unacceptable toxicity, withdrawal of consent or death whichever occurs first.

Arm type	Experimental

Investigational medicinal product name	Bevacizumab
Investigational medicinal product code	
Other name	Avastin
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Bevacizumab will be administered at 7.5 or 15 milligrams per kilogram (mg/kg) intravenously every 3 weeks (Q3W), or 5 or 10 mg/kg intravenously every 2 weeks (Q2W).

Arm title	Renal Cell Carcinoma

Arm description:

Participants will receive bevacizumab until progression of disease or unacceptable toxicity, withdrawal of consent or death whichever occurs first.

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

Dosage and administration details:

Bevacizumab will be administered at 7.5 or 15 milligrams per kilogram (mg/kg) intravenously every 3 weeks (Q3W), or 5 or 10 mg/kg intravenously every 2 weeks (Q2W).

Arm title	Non-Squamous, Non-Small Cell Lung Cancer

Arm description:

Participants will receive bevacizumab until progression of disease or unacceptable toxicity, withdrawal of consent or death whichever occurs first.

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

Dosage and administration details:

Bevacizumab will be administered at 7.5 or 15 milligrams per kilogram (mg/kg) intravenously every 3 weeks (Q3W), or 5 or 10 mg/kg intravenously every 2 weeks (Q2W).

Arm title	Glioblastoma Multiforme

Arm description:

Participants will receive bevacizumab until progression of disease or unacceptable toxicity, withdrawal of consent or death whichever occurs first.

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

Dosage and administration details:

Bevacizumab will be administered at 7.5 or 15 milligrams per kilogram (mg/kg) intravenously every 3 weeks (Q3W), or 5 or 10 mg/kg intravenously every 2 weeks (Q2W).

Number of subjects in period 1	Breast Cancer	Ovarian Cancer or Peritoneal Carcinoma	Colorectal Cancer
Started	11	41	7
Completed	8	28	5
Not completed	3	13	2
Adverse event, serious fatal	1	-	-
change in treatment	-	6	2
Consent withdrawn by subject	2	4	-
multiple reasons	-	3	-

Number of subjects in period 1	Renal Cell Carcinoma	Non-Squamous, Non-Small Cell Lung Cancer	Glioblastoma Multiforme
Started	6	16	14
Completed	3	14	10
Not completed	3	2	4
Adverse event, serious fatal	1	1	1
change in treatment	-	1	3
Consent withdrawn by subject	1	-	-
multiple reasons	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Breast Cancer
Reporting group description:	
Participants will receive bevacizumab until progression of disease or unacceptable toxicity, withdrawal of consent or death whichever occurs first.	
Reporting group title	Ovarian Cancer or Peritoneal Carcinoma
Reporting group description:	
Participants will receive bevacizumab until progression of disease or unacceptable toxicity, withdrawal of consent or death whichever occurs first.	
Reporting group title	Colorectal Cancer
Reporting group description:	
Participants will receive bevacizumab until progression of disease or unacceptable toxicity, withdrawal of consent or death whichever occurs first.	
Reporting group title	Renal Cell Carcinoma
Reporting group description:	
Participants will receive bevacizumab until progression of disease or unacceptable toxicity, withdrawal of consent or death whichever occurs first.	
Reporting group title	Non-Squamous, Non-Small Cell Lung Cancer
Reporting group description:	
Participants will receive bevacizumab until progression of disease or unacceptable toxicity, withdrawal of consent or death whichever occurs first.	
Reporting group title	Glioblastoma Multiforme
Reporting group description:	
Participants will receive bevacizumab until progression of disease or unacceptable toxicity, withdrawal of consent or death whichever occurs first.	

Reporting group values	Breast Cancer	Ovarian Cancer or Peritoneal Carcinoma	Colorectal Cancer
Number of subjects	11	41	7
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	9	30	3
From 65-84 years	2	11	4
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	54.5	56.7	66.7
standard deviation	± 7.3	± 11.2	± 13.9
Sex: Female, Male Units:			
Female	11	41	3

Male	0	0	4

Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	0	0	0
More than one race	0	0	0
Unknown or Not Reported	11	41	7

Reporting group values	Renal Cell Carcinoma	Non-Squamous, Non-Small Cell Lung Cancer	Glioblastoma Multiforme
Number of subjects	6	16	14
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	2	11	13
From 65-84 years	4	5	1
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	63.5	58.5	49.5
standard deviation	± 9.8	± 10.5	± 10.9
Sex: Female, Male Units:			
Female	2	6	4
Male	4	10	10
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	0	0	0
More than one race	0	0	0
Unknown or Not Reported	6	16	14

Reporting group values	Total		
Number of subjects	95		

Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	68		
From 65-84 years	27		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units:			
Female	67		
Male	28		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	0		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	0		
More than one race	0		
Unknown or Not Reported	95		

End points

End points reporting groups

Reporting group title	Breast Cancer
Reporting group description:	
Participants will receive bevacizumab until progression of disease or unacceptable toxicity, withdrawal of consent or death whichever occurs first.	
Reporting group title	Ovarian Cancer or Peritoneal Carcinoma
Reporting group description:	
Participants will receive bevacizumab until progression of disease or unacceptable toxicity, withdrawal of consent or death whichever occurs first.	
Reporting group title	Colorectal Cancer
Reporting group description:	
Participants will receive bevacizumab until progression of disease or unacceptable toxicity, withdrawal of consent or death whichever occurs first.	
Reporting group title	Renal Cell Carcinoma
Reporting group description:	
Participants will receive bevacizumab until progression of disease or unacceptable toxicity, withdrawal of consent or death whichever occurs first.	
Reporting group title	Non-Squamous, Non-Small Cell Lung Cancer
Reporting group description:	
Participants will receive bevacizumab until progression of disease or unacceptable toxicity, withdrawal of consent or death whichever occurs first.	
Reporting group title	Glioblastoma Multiforme
Reporting group description:	
Participants will receive bevacizumab until progression of disease or unacceptable toxicity, withdrawal of consent or death whichever occurs first.	

Primary: Percentage of Participants With Adverse Events

End point title	Percentage of Participants With Adverse Events[1]
End point description:	
An adverse event (AE) is any untoward medical occurrence in a participant or clinical investigation participant administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not considered related to the medicinal (investigational) product.	
End point type	Primary
End point timeframe:	
Baseline up to approximately 81 months	

Notes:

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

End point values	Breast Cancer	Ovarian Cancer or Peritoneal Carcinoma	Colorectal Cancer	Renal Cell Carcinoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	41	7	6
Units: percentage of participants				
number (not applicable)	90.9	78.0	71.4	100.0

End point values	Non-Squamous, Non-Small Cell Lung Cancer	Glioblastoma Multiforme		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: percentage of participants				
number (not applicable)	75.0	83.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

Progression free survival is defined as the time from first dose of Bevacizumab in this extension trial (E-trial) to the time of first documented disease progression or death due to any cause, whichever occurs first.

End point type	Secondary

End point timeframe:

Baseline up to approximately 81 months

End point values	Breast Cancer	Ovarian Cancer or Peritoneal Carcinoma	Colorectal Cancer	Renal Cell Carcinoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	41	7	6
Units: months				
arithmetic mean (standard deviation)	35.31 (± 23.809)	24.39 (± 19.759)	17.98 (± 24.202)	9.31 (± 12.046)

End point values	Non-Squamous, Non-Small Cell Lung Cancer	Glioblastoma Multiforme		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: months				
arithmetic mean (standard deviation)	17.14 (± 14.152)	11.31 (± 10.301)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Overall survival time is defined as the time from first dose of Bevacizumab in this E-trial to death from any cause.

End point type	Secondary

End point timeframe:

Baseline up to approximately 81 months

End point values	Breast Cancer	Ovarian Cancer or Peritoneal Carcinoma	Colorectal Cancer	Renal Cell Carcinoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	41	7	6
Units: months				
arithmetic mean (standard deviation)	38.82 (± 24.159)	27.35 (± 20.020)	20.30 (± 23.761)	11.98 (± 10.950)

End point values	Non-Squamous, Non-Small Cell Lung Cancer	Glioblastoma Multiforme		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: months				
arithmetic mean (standard deviation)	18.31 (± 14.962)	12.99 (± 10.795)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to approximately 81 months	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	Breast Cancer
Reporting group description:	
Participants will receive bevacizumab until progression of disease or unacceptable toxicity, withdrawal of consent or death whichever occurs first.	
Reporting group title	Colorectal Cancer
Reporting group description:	
Participants will receive bevacizumab until progression of disease or unacceptable toxicity, withdrawal of consent or death whichever occurs first.	
Reporting group title	Glioblastoma Multiforme
Reporting group description:	
Participants will receive bevacizumab until progression of disease or unacceptable toxicity, withdrawal of consent or death whichever occurs first.	
Reporting group title	Non-Squamous, Non-Small Cell Lung Cancer
Reporting group description:	
Participants will receive bevacizumab until progression of disease or unacceptable toxicity, withdrawal of consent or death whichever occurs first.	
Reporting group title	Ovarian Cancer or Peritoneal Carcinoma
Reporting group description:	
Participants will receive bevacizumab until progression of disease or unacceptable toxicity, withdrawal of consent or death whichever occurs first.	
Reporting group title	Renal Cell Carcinoma
Reporting group description:	
Participants will receive bevacizumab until progression of disease or unacceptable toxicity, withdrawal of consent or death whichever occurs first.	

Serious adverse events	Breast Cancer	Colorectal Cancer	Glioblastoma Multiforme
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 11 (18.18%)	2 / 7 (28.57%)	3 / 14 (21.43%)
number of deaths (all causes)	1	0	1
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
FEMUR FRACTURE			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FRACTURE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
JAW FRACTURE			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
AORTIC STENOSIS			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
CIRCULATORY COLLAPSE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTENSIVE CRISIS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
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			
CARDIAC FAILURE			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SINUS BRADYCARDIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
ISCHAEMIC STROKE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRANSIENT ISCHAEMIC ATTACK			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
VERTIGO			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 14 (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
Gastrointestinal disorders			
VOMITING			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
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			
PNEUMONITIS			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
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			
NEPHROTIC SYNDROME			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
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			
APPENDICITIS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COMPLICATED APPENDICITIS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFECTION			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 14 (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
MENINGITIS BACTERIAL			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND INFECTION			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
DEHYDRATION			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
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	Non-Squamous, Non-Small Cell Lung Cancer	Ovarian Cancer or Peritoneal Carcinoma	Renal Cell Carcinoma
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 16 (31.25%)	2 / 41 (4.88%)	3 / 6 (50.00%)
number of deaths (all causes)	1	0	1
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
FEMUR FRACTURE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FRACTURE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
JAW FRACTURE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
AORTIC STENOSIS			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CIRCULATORY COLLAPSE			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (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
HYPERTENSIVE CRISIS			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (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
Cardiac disorders			
CARDIAC FAILURE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SINUS BRADYCARDIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
ISCHAEMIC STROKE			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (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
TRANSIENT ISCHAEMIC ATTACK			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
VERTIGO			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
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			
VOMITING			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (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
Respiratory, thoracic and mediastinal disorders			
PNEUMONITIS			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
NEPHROTIC SYNDROME			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 41 (2.44%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
APPENDICITIS			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (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
COMPLICATED APPENDICITIS			

alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (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
INFECTION			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENINGITIS BACTERIAL			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND INFECTION			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
DEHYDRATION			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 41 (2.44%)	0 / 6 (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

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

Non-serious adverse events	Breast Cancer	Colorectal Cancer	Glioblastoma Multiforme
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 11 (90.91%)	5 / 7 (71.43%)	14 / 14 (100.00%)
Vascular disorders			

EMBOLISM VENOUS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
HYPERTENSION			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 11 (18.18%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	3	0	0
LYMPHOEDEMA			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Surgical and medical procedures			
TOOTH EXTRACTION			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
ASTHENIA			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 11 (36.36%)	0 / 7 (0.00%)	5 / 14 (35.71%)
occurrences (all)	5	0	6
CHEST PAIN			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
FATIGUE			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	1 / 7 (14.29%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
MUCOSAL INFLAMMATION			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
OEDEMA			

alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
OEDEMA PERIPHERAL			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
PAIN			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
PYREXIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	2 / 14 (14.29%)
occurrences (all)	0	0	2
Immune system disorders			
CONTRAST MEDIA ALLERGY			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
SEASONAL ALLERGY			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
CYSTOCELE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
ERECTILE DYSFUNCTION			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
UTERINE PROLAPSE			
alternative assessment type:			

Systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
COUGH			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 11 (36.36%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	5	0	1
DYSPHONIA			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
DYSPNOEA			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 11 (18.18%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	4	0	0
EPISTAXIS			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	2 / 14 (14.29%)
occurrences (all)	1	0	3
OROPHARYNGEAL PAIN			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
PRODUCTIVE COUGH			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
RHINORRHOEA			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 11 (18.18%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Psychiatric disorders			

IRRITABILITY			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	3	0	2
AMYLASE INCREASED			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	3	0	0
ASPARTATE AMINOTRANSFERASE INCREASED			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 11 (18.18%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	3	0	0
BLOOD ALKALINE PHOSPHATASE INCREASED			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	3	0	0
BLOOD BILIRUBIN INCREASED			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	1 / 7 (14.29%)	0 / 14 (0.00%)
occurrences (all)	1	2	0
BLOOD CREATININE INCREASED			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
BLOOD PRESSURE INCREASED			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	2 / 14 (14.29%)
occurrences (all)	0	0	3
EJECTION FRACTION DECREASED			

alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 11 (18.18%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	8	0	0
LIPASE INCREASED			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
PLATELET COUNT DECREASED			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	2 / 14 (14.29%)
occurrences (all)	0	0	3
WEIGHT DECREASED			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
WEIGHT INCREASED			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
ANKLE FRACTURE			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
FALL			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
INCISION SITE PAIN			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
RADIUS FRACTURE			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
BUNDLE BRANCH BLOCK RIGHT			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
CONGESTIVE CARDIOMYOPATHY			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
APHONIA			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
COMPLEX REGIONAL PAIN SYNDROME			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
DIZZINESS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
DYSAESTHESIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
DYSTONIA			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
FACIAL NEURALGIA			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
HEADACHE			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 11 (27.27%)	1 / 7 (14.29%)	6 / 14 (42.86%)
occurrences (all)	5	1	7
HYPOAESTHESIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
MIGRAINE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
MOVEMENT DISORDER			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
NERVOUS SYSTEM DISORDER			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
NEUROPATHY PERIPHERAL			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
NEUROTOXICITY			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0

PARAESTHESIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
PERIPHERAL SENSORY NEUROPATHY			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
SCIATICA			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
SEIZURE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
SOMNOLENCE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
ANAEMIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
LEUKOPENIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 14 (0.00%)
occurrences (all)	0	3	0
NEUTROPENIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 14 (0.00%)
occurrences (all)	0	12	0
NEUTROPHILIA			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
THROMBOCYTOPENIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	2 / 14 (14.29%)
occurrences (all)	0	0	2
Ear and labyrinth disorders			
EAR PAIN			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
VERTIGO			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
CONJUNCTIVAL HAEMORRHAGE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
LACRIMATION INCREASED			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	1 / 7 (14.29%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
PERIORBITAL DISORDER			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
XEROPHTHALMIA			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
ABDOMINAL PAIN			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 11 (9.09%)	1 / 7 (14.29%)	0 / 14 (0.00%)
occurrences (all)	21	1	0
ABDOMINAL PAIN UPPER			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
CHEILITIS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 14 (0.00%)
occurrences (all)	0	3	0
CONSTIPATION			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
DENTAL CARIES			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
DIARRHOEA			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 11 (18.18%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	2	0	2
DYSPEPSIA			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
GASTRITIS EROSIVE			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
GINGIVAL BLEEDING			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	2 / 14 (14.29%)
occurrences (all)	0	0	2

MOUTH ULCERATION			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
NAUSEA			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 11 (18.18%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	2	0	1
ORAL PAIN			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
PEPTIC ULCER			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
STOMATITIS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
TOOTHACHE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
VOMITING			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 11 (18.18%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Skin and subcutaneous tissue disorders			
ALOPECIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
ERYTHEMA			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
ONYCHOLYSIS			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
PALMAR-PLANTAR ERYTHRODYSAESTHESIA SYNDROME			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	1 / 7 (14.29%)	0 / 14 (0.00%)
occurrences (all)	1	4	0
RASH			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
RASH MACULAR			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
SKIN SWELLING			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
PROTEINURIA			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 11 (54.55%)	2 / 7 (28.57%)	5 / 14 (35.71%)
occurrences (all)	55	5	15
RENAL FAILURE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
RENAL IMPAIRMENT			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
URINARY INCONTINENCE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 11 (18.18%)	1 / 7 (14.29%)	2 / 14 (14.29%)
occurrences (all)	2	1	2
BACK PAIN			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
MUSCLE SPASMS			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 11 (18.18%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	6	0	0
MUSCULOSKELETAL DISCOMFORT			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
MUSCULOSKELETAL PAIN			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 11 (36.36%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	7	0	0
MYALGIA			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
NECK PAIN			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	2
OSTEOARTHRITIS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
PAIN IN EXTREMITY			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
PERIARTHRITIS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
SPINAL PAIN			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
BACTERIURIA			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
BREAST DISCHARGE INFECTED			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
BRONCHITIS			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	1 / 7 (14.29%)	1 / 14 (7.14%)
occurrences (all)	1	1	1
CONJUNCTIVITIS			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
CYSTITIS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
DIVERTICULITIS			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
EAR INFECTION			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
INFLUENZA			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
LACRIMAL GLAND ABSCESS			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
NAIL INFECTION			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
NASOPHARYNGITIS			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	1 / 7 (14.29%)	1 / 14 (7.14%)
occurrences (all)	3	1	1
PERIODONTITIS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 7 (14.29%)	0 / 14 (0.00%)
occurrences (all)	0	1	0

RESPIRATORY TRACT INFECTION			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
RHINITIS			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
SINUSITIS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
TOOTH ABSCESS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
TOOTH INFECTION			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	3	0	1
UPPER RESPIRATORY TRACT INFECTION			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 11 (18.18%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
URINARY TRACT INFECTION			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
VIRAL UPPER RESPIRATORY TRACT INFECTION			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Metabolism and nutrition disorders			

DECREASED APPETITE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
GOUT			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
HYPERGLYCAEMIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
HYPOALBUMINAEMIA			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
HYPOCALCAEMIA			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
HYPOKALAEMIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
HYPONATRAEMIA			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 11 (18.18%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
IRON DEFICIENCY			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 7 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Non-Squamous, Non-Small Cell Lung Cancer	Ovarian Cancer or Peritoneal Carcinoma	Renal Cell Carcinoma

Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 16 (75.00%)	31 / 41 (75.61%)	6 / 6 (100.00%)
Vascular disorders			
EMBOLISM VENOUS			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
HYPERTENSION			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	7 / 41 (17.07%)	2 / 6 (33.33%)
occurrences (all)	1	25	5
LYMPHOEDEMA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
TOOTH EXTRACTION			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
ASTHENIA			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 16 (18.75%)	3 / 41 (7.32%)	0 / 6 (0.00%)
occurrences (all)	5	5	0
CHEST PAIN			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	2 / 41 (4.88%)	0 / 6 (0.00%)
occurrences (all)	1	3	0
FATIGUE			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	4 / 41 (9.76%)	0 / 6 (0.00%)
occurrences (all)	1	6	0
MUCOSAL INFLAMMATION			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 16 (6.25%)	2 / 41 (4.88%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
OEDEMA			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
OEDEMA PERIPHERAL			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 16 (12.50%)	4 / 41 (9.76%)	0 / 6 (0.00%)
occurrences (all)	3	7	0
PAIN			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
PYREXIA			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	1 / 41 (2.44%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Immune system disorders			
CONTRAST MEDIA ALLERGY			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
SEASONAL ALLERGY			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
CYSTOCELE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
ERECTILE DYSFUNCTION			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
UTERINE PROLAPSE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
COUGH			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 41 (2.44%)	1 / 6 (16.67%)
occurrences (all)	0	2	1
DYSPHONIA			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	1 / 41 (2.44%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
DYSPNOEA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
EPISTAXIS			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 16 (12.50%)	1 / 41 (2.44%)	0 / 6 (0.00%)
occurrences (all)	3	1	0
OROPHARYNGEAL PAIN			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
PRODUCTIVE COUGH			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
RHINORRHOEA			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
IRRITABILITY			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	2 / 41 (4.88%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
AMYLASE INCREASED			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
ASPARTATE AMINOTRANSFERASE INCREASED			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	2 / 41 (4.88%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
BLOOD ALKALINE PHOSPHATASE INCREASED			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	2 / 41 (4.88%)	0 / 6 (0.00%)
occurrences (all)	0	9	0
BLOOD BILIRUBIN INCREASED			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
BLOOD CREATININE INCREASED			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	5 / 41 (12.20%)	0 / 6 (0.00%)
occurrences (all)	0	10	0
BLOOD PRESSURE INCREASED			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
EJECTION FRACTION DECREASED			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
LIPASE INCREASED			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
PLATELET COUNT DECREASED			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
WEIGHT DECREASED			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 16 (12.50%)	1 / 41 (2.44%)	0 / 6 (0.00%)
occurrences (all)	3	1	0
WEIGHT INCREASED			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
ANKLE FRACTURE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
FALL			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 16 (0.00%)	1 / 41 (2.44%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
INCISION SITE PAIN			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
RADIUS FRACTURE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
BUNDLE BRANCH BLOCK RIGHT			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
CONGESTIVE CARDIOMYOPATHY			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
APHONIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
COMPLEX REGIONAL PAIN SYNDROME			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
DIZZINESS			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	3 / 41 (7.32%)	0 / 6 (0.00%)
occurrences (all)	1	3	0
DYSAESTHESIA			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
DYSTONIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
FACIAL NEURALGIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
HEADACHE			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	4 / 41 (9.76%)	0 / 6 (0.00%)
occurrences (all)	1	6	0
HYPOAESTHESIA			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
MIGRAINE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
MOVEMENT DISORDER			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
NERVOUS SYSTEM DISORDER			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
NEUROPATHY PERIPHERAL			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0

NEUROTOXICITY			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
PARAESTHESIA			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 16 (12.50%)	2 / 41 (4.88%)	0 / 6 (0.00%)
occurrences (all)	2	2	0
PERIPHERAL SENSORY NEUROPATHY			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
SCIATICA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
SEIZURE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
SOMNOLENCE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 41 (2.44%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
ANAEMIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	5 / 41 (12.20%)	0 / 6 (0.00%)
occurrences (all)	0	20	0
LEUKOPENIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	2 / 41 (4.88%)	0 / 6 (0.00%)
occurrences (all)	0	7	0
NEUTROPENIA			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 16 (0.00%)	3 / 41 (7.32%)	0 / 6 (0.00%)
occurrences (all)	0	9	0
NEUTROPHILIA			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
THROMBOCYTOPENIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	3 / 41 (7.32%)	0 / 6 (0.00%)
occurrences (all)	0	10	0
Ear and labyrinth disorders			
EAR PAIN			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
VERTIGO			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
CONJUNCTIVAL HAEMORRHAGE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
LACRIMATION INCREASED			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
PERIORBITAL DISORDER			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
XEROPHTHALMIA			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
ABDOMINAL PAIN			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	2 / 41 (4.88%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
ABDOMINAL PAIN UPPER			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 41 (2.44%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
CHEILITIS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
CONSTIPATION			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	1 / 41 (2.44%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
DENTAL CARIES			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	2 / 41 (4.88%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
DIARRHOEA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	7 / 41 (17.07%)	0 / 6 (0.00%)
occurrences (all)	0	19	0
DYSPEPSIA			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
GASTRITIS EROSIVE			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
GINGIVAL BLEEDING			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 41 (2.44%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
MOUTH ULCERATION			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
NAUSEA			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 16 (18.75%)	5 / 41 (12.20%)	0 / 6 (0.00%)
occurrences (all)	7	8	0
ORAL PAIN			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
PEPTIC ULCER			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
STOMATITIS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
TOOTHACHE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
VOMITING			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	5 / 41 (12.20%)	1 / 6 (16.67%)
occurrences (all)	0	5	1

Skin and subcutaneous tissue disorders			
ALOPECIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
ERYTHEMA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
ONYCHOLYSIS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
PALMAR-PLANTAR ERYTHRODYSAESTHESIA SYNDROME			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
RASH			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 16 (12.50%)	1 / 41 (2.44%)	0 / 6 (0.00%)
occurrences (all)	3	1	0
RASH MACULAR			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
SKIN SWELLING			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
PROTEINURIA			
alternative assessment type: Systematic			
subjects affected / exposed	8 / 16 (50.00%)	20 / 41 (48.78%)	1 / 6 (16.67%)
occurrences (all)	26	100	1
RENAL FAILURE			

alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
RENAL IMPAIRMENT			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
URINARY INCONTINENCE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 41 (2.44%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
BACK PAIN			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	5 / 41 (12.20%)	0 / 6 (0.00%)
occurrences (all)	0	5	0
MUSCLE SPASMS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 41 (2.44%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
MUSCULOSKELETAL DISCOMFORT			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
MUSCULOSKELETAL PAIN			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	2 / 41 (4.88%)	0 / 6 (0.00%)
occurrences (all)	2	2	0
MYALGIA			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 16 (0.00%)	1 / 41 (2.44%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
NECK PAIN			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
OSTEOARTHRITIS			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
PAIN IN EXTREMITY			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 41 (2.44%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
PERIARTHRITIS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
SPINAL PAIN			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
BACTERIURIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
BREAST DISCHARGE INFECTED			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
BRONCHITIS			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
CONJUNCTIVITIS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
CYSTITIS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
DIVERTICULITIS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
EAR INFECTION			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
INFLUENZA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	2 / 41 (4.88%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
LACRIMAL GLAND ABSCESS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
NAIL INFECTION			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
NASOPHARYNGITIS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

PERIODONTITIS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
RESPIRATORY TRACT INFECTION			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	2 / 41 (4.88%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
RHINITIS			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
SINUSITIS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 41 (2.44%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
TOOTH ABSCESS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	3 / 41 (7.32%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
TOOTH INFECTION			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
UPPER RESPIRATORY TRACT INFECTION			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 16 (6.25%)	2 / 41 (4.88%)	0 / 6 (0.00%)
occurrences (all)	1	4	0
URINARY TRACT INFECTION			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	9 / 41 (21.95%)	1 / 6 (16.67%)
occurrences (all)	0	26	1
VIRAL UPPER RESPIRATORY TRACT INFECTION			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 16 (12.50%)	3 / 41 (7.32%)	0 / 6 (0.00%)
occurrences (all)	2	4	0
GOUT			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
HYPERGLYCAEMIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	3 / 41 (7.32%)	0 / 6 (0.00%)
occurrences (all)	0	15	0
HYPOALBUMINAEMIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	4 / 41 (9.76%)	0 / 6 (0.00%)
occurrences (all)	0	11	0
HYPOCALCAEMIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 41 (2.44%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
HYPOKALAEMIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 41 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
HYPONATRAEMIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 41 (2.44%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
IRON DEFICIENCY			
alternative assessment type: Systematic			

subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 41 (0.00%) 0	0 / 6 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 February 2013	Major changes included a change to study personnel and clarification of study phase.
08 November 2018	Changes to provide for transition of patients from supply of bevacizumab via this clinical study to commercial and Post-Trial Access Program supplies

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported