Clinical trial results:
Phase 2 Open-label Multicenter Study to Evaluate the Safety and Efficacy of Sunitinib Malate in Combination With AMG 386 as First Line or Second Line Therapy for Subjects With Metastatic Renal Cell Carcinoma

Summary

EudraCT number	2008-006210-14
Trial protocol	BE FR
Global end of trial date	25 June 2019

Results information

Result version number	v1 (current)
This version publication date	25 June 2020
First version publication date	25 June 2020

Trial information

Trial identification

Sponsor protocol code	20080579

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00853372
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 June 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 June 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to determine the safety and tolerability of trebananib in combination with sunitinib in subjects with metastatic renal cell carcinoma (mRCC).

Protection of trial subjects:

This study was conducted in accordance with United States Food and Drug Administration (FDA) regulations/guidelines set forth in 21 Code of Federal Regulations (CFR) Parts 11, 50, 54, 56, and 312, and International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines.
Before a subject could enter study or any study-specific procedures could be performed, the investigator was required to obtain 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. A separate informed consent form was required if a subject was to participate in the optional pharmacogenetics portion of the study.

Background therapy:

Sunitinib (SUTENT [oral multi-kinase inhibitor]) was administered 50 mg QD and was considered to be the background therapy as it is licensed for treatment of RCC and was administered to all subjects.

Evidence for comparator: -

Actual start date of recruitment	28 May 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 19
Country: Number of subjects enrolled	Australia: 7
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	France: 34
Country: Number of subjects enrolled	Poland: 22
Worldwide total number of subjects	85
EEA total number of subjects	59

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	57
From 65 to 84 years	28
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 18 sites in the United States, Australia, Belgium, France, and Poland. The first participant was enrolled on 28 May 2009. The last participant was enrolled on 29 November 2010.

Pre-assignment

Screening details:

All participants had screening procedures completed within 28 days prior to enrollment.

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	Trebananib 10 mg/kg + Sunitinib

Arm description:

Trebananib 10 mg/kg intravenously (IV) once weekly (QW) plus sunitinib 50 mg orally (PO) once daily (QD) 4 weeks on/2 weeks off

Arm type	Experimental
Investigational medicinal product name	trebananib
Investigational medicinal product code	AMG 386
Other name	Angiogenesis inhibitor
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Treatment with trebananib was to continue until disease progression, clinical progression, unacceptable toxicity, withdrawal of consent, or death.

Arm title	Trebananib 15 mg/kg + Sunitinib

Arm description:

Trebananib 15 mg/kg IV QW plus sunitinib 50 mg PO QD 4 weeks on/2 weeks off

Arm type	Experimental
Investigational medicinal product name	trebananib
Investigational medicinal product code	AMG 386
Other name	Angiogenesis inhibitor
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Treatment with trebananib was to continue until disease progression, clinical progression, unacceptable toxicity, withdrawal of consent, or death.

Number of subjects in period 1	Trebananib 10 mg/kg + Sunitinib	Trebananib 15 mg/kg + Sunitinib
Started	43	42
Completed	11	13
Not completed	32	29
Adverse event, serious fatal	30	26
Full Consent Withdrawn	1	1
Lost to follow-up	1	2

Baseline characteristics

Reporting groups	
Reporting group title	Trebananib 10 mg/kg + Sunitinib
Reporting group description:	
Trebananib 10 mg/kg intravenously (IV) once weekly (QW) plus sunitinib 50 mg orally (PO) once daily (QD) 4 weeks on/2 weeks off	
Reporting group title	Trebananib 15 mg/kg + Sunitinib
Reporting group description:	
Trebananib 15 mg/kg IV QW plus sunitinib 50 mg PO QD 4 weeks on/2 weeks off	

Reporting group values	Trebananib 10 mg/kg + Sunitinib	Trebananib 15 mg/kg + Sunitinib	Total
Number of subjects	43	42	85
Age Categorical Units: participants			
Age continuous Units: years			
arithmetic mean	58.3	61.4	
standard deviation	± 9.7	± 8.5	-
Sex: Female, Male Units:			
Female	5	10	15
Male	38	32	70
Race/Ethnicity, Customized Units: Subjects			
White or Caucasian	41	42	83
Black or African American	1	0	1
Hispanic or Latino	1	0	1
Asian	0	0	0
Japanese	0	0	0
American Indian or Alaska Native	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Aborigine	0	0	0
Other, Not Specified	0	0	0

End points

End points reporting groups

Reporting group title	Trebananib 10 mg/kg + Sunitinib
Reporting group description:	
Trebananib 10 mg/kg intravenously (IV) once weekly (QW) plus sunitinib 50 mg orally (PO) once daily (QD) 4 weeks on/2 weeks off	
Reporting group title	Trebananib 15 mg/kg + Sunitinib
Reporting group description:	
Trebananib 15 mg/kg IV QW plus sunitinib 50 mg PO QD 4 weeks on/2 weeks off	

Primary: Number of Participants with Treatment-Emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs), and Discontinuations (DCs) Due to Adverse Events (AEs)

End point title	Number of Participants with Treatment-Emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs), and Discontinuations (DCs) Due to Adverse Events (AEs)[1]

End point description:

AE: any untoward medical occurrence that does not necessarily have a causal relationship with treatment. SAE: an AE that: is fatal; is life threatening; requires in-patient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect; is an other significant medical hazard. Treatment-emergent AEs (TEAEs) are those that occurred after the first administration of study drug through 30 days after the last study drug administration. Severity was graded according to Common Terminology Criteria (CTCAE) version 3.0, as grade 1 (mild), grade 2 (moderate), grade 3 (severe), grade 4 (life-threatening), grade 5 (death).
Safety Analysis Set: all participants who received at least 1 dose of trebananib and 1 dose of sunitinib.

End point type	Primary

End point timeframe:

From first dose of study drug to 30 days after last dose. Median treatment duration of trebananib and sunitinib was 316 and 315 days, respectively, for Trebananib 10 mg/kg+Sunitinib, and 393 and 358 days, respectively, for Trebananib 15 mg/kg+Sunitinib.

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 are presented per protocol.

End point values	Trebananib 10 mg/kg + Sunitinib	Trebananib 15 mg/kg + Sunitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	42		
Units: participants				
TEAEs, All	43	42		
TEAEs, Grade ≥ 3	32	34		
TEAEs, Grade ≥ 4	4	7		
TEAEs, Fatal AEs	1	1		
TEAEs, SAEs	17	26		
TEAEs Leading to () DC of Trebananib	7	14		
TEAEs DC of Trebananib, Serious	5	12		
TEAEs DC of Trebananib, Non-Serious	2	2		
TEAEs DC of Sunitinib	9	16		
TEAEs DC of Sunitinib, Serious	5	12		

TEAEs DC of Sunitinib, Non-Serious	4	5		
TEAEs DC of All Treatment	6	14		
TEAEs DC of All Treatment, Serious	5	12		
TEAEs DC of All Treatment, Non-Serious	1	2		
Treatment-Related (TR) TEAEs, All	43	42		
TR TEAEs, Grade ≥ 3	25	31		
TR TEAEs, Grade ≥ 4	2	5		
TR TEAEs, Fatal AEs	0	1		
TR TEAEs, SAEs	11	18		
TR TEAEs DC of Trebananib	6	13		
TR TEAEs DC of Trebananib, Serious	4	11		
TR TEAEs DC of Trebananib, Non-Serious	2	2		
TR TEAEs DC of Sunitinib	8	15		
TR TEAEs DC of Sunitinib, Serious	4	11		
TR TEAEs DC of Sunitinib, Non-Serious	4	5		
TR TEAEs DC of All Treatment	5	13		
TR TEAEs DC of All Treatment, Serious	4	11		
TR TEAEs DC of All Treatment, Non-Serious	1	2		
Trebananib-Related (TrR) TEAEs, All	34	39		
TrR TEAEs, Grade ≥ 3	17	19		
TrR TEAEs, Grade ≥ 4	1	4		
TrR TEAEs, Fatal AEs	0	1		
TrR TEAEs, SAEs	10	15		
TrR TEAEs DC of Trebananib	6	13		
TrR TEAEs DC of Trebananib, Serious	4	11		
TrR TEAEs DC of Trebananib, Non-Serious	2	2		
TrR TEAEs DC of Sunitinib	6	13		
TrR TEAEs DC of Sunitinib, Serious	4	11		
TrR TEAEs DC of Sunitinib, Non-Serious	2	3		
TrR TEAEs DC of All Treatment	5	13		
TrR TEAEs DC of All Treatment, Serious	4	11		
TrR TEAEs DC of All Treatment, Non-Serious	1	2		
Sunitinib-Related (SR) TEAEs, All	43	42		
SR TEAEs, Grade ≥ 3	25	31		
SR TEAEs, Grade ≥ 4	2	5		
SR TEAEs, Fatal AEs	0	1		
SR TEAEs, SAEs	9	15		
SR TEAEs DC of Trebananib	4	11		
SR TEAEs DC of Trebananib, Serious	3	10		
SR TEAEs DC of Trebananib, Non-Serious	1	1		
SR TEAEs DC Sunitinib	7	13		
SR TEAEs DC of Sunitinib, Serious	3	10		
SR TEAEs DC of Sunitinib, Non-Serious	4	4		
SR TEAEs DC of All Treatment	4	11		

SR TEAEs DC of All Treatment, Serious	3	10		
SR TEAEs DC of All Treatment, Non-Serious	1	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Dose Delays Due to Adverse Events

End point title	Number of Participants With Dose Delays Due to Adverse Events[2]

End point description:

A trebananib dose was considered delayed if it was administered 11 or more days from the previous trebananib infusion. A sunitinib dose was considered delayed if it was administered 3 or more days from the previous dose, except during holidays.
Safety Analysis Set: participants who received at least 1 dose of trebananib and 1 dose of sunitinib.

End point type	Primary

End point timeframe:

Median treatment duration of trebananib and sunitinib was 316 and 315 days, respectively, for Trebananib 10 mg/kg+Sunitinib, and 393 and 358 days, respectively, for Trebananib 15 mg/kg+Sunitinib.

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: Descriptive statistics are presented per protocol.

End point values	Trebananib 10 mg/kg + Sunitinib	Trebananib 15 mg/kg + Sunitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	42		
Units: participants				
Trebananib dose delays	26	28		
Sunitinib dose delays	29	27		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Sunitinib Dose Modifications Within 12 Weeks of First Dose

End point title	Number of Participants With Sunitinib Dose Modifications Within 12 Weeks of First Dose[3]

End point description:

Participants who had a sunitinib dose modification within 12 weeks from their first dose due to adverse event, laboratory toxicity, or laboratory toxicity and adverse event.
Safety Analysis Set: all participants who received at least 1 dose of trebananib and 1 dose of sunitinib.

End point type	Primary

End point timeframe:

first 12 weeks of study treatment

Notes:

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

End point values	Trebananib 10 mg/kg + Sunitinib	Trebananib 15 mg/kg + Sunitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	42		
Units: participants				
Any Dose Modification (DM)	25	24		
DM Due to Adverse Event	20	18		
DM Due to Laboratory Toxicity	4	4		
DM Due to Laboratory Toxicity and Adverse Event	1	2		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Worst Post-Baseline Grade 3 or Higher Toxicity in Laboratory Values

End point title	Number of Participants With Worst Post-Baseline Grade 3 or Higher Toxicity in Laboratory Values[4]

End point description:

Severity was graded according to Common Terminology Criteria (CTCAE) version 3.0, as grade 1 (mild), grade 2 (moderate), grade 3 (severe), grade 4 (life-threatening), grade 5 (death).
Safety Analysis Set: all participants who received at least 1 dose of trebananib and 1 dose of sunitinib.

End point type	Primary

End point timeframe:

From first dose of study drug to 30 days after last dose. Median treatment duration of trebananib and sunitinib was 316 and 315 days, respectively, for Trebananib 10 mg/kg+Sunitinib, and 393 and 358 days, respectively, for Trebananib 15 mg/kg+Sunitinib.

Notes:

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

End point values	Trebananib 10 mg/kg + Sunitinib	Trebananib 15 mg/kg + Sunitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	42		
Units: participants				
Alanine Aminotransferase, Above Normal (AN)	3	2		
Albumin, Below Normal (BN)	1	1		
Alkaline Phosphatase, AN	0	2		
Amylase, AN	2	5		
Aspartate Aminotransferase, AN	2	2		
Glucose, AN	1	3		
Glucose, BN	1	0		

Lipase, AN	5	7		
Magnesium, BN	0	1		
Phosphorus, BN	3	4		
Potassium, BN	2	2		
Sodium, BN	1	4		
Total Bilirubin, AN	0	2		
Absolute Neutrophil Count, BN	3	5		
Hemoglobin, BN	1	3		
Lymphocytes, BN	6	3		
Partial Thromboplastin Time, AN	1	1		
Platelets, BN	3	2		
Total Neutrophils, BN	3	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)

End point description:

ORR was defined as the percentage of participants with either a confirmed complete response (CR) or partial response (PR) per modified Response Evaluation Criteria in Solid Tumor (RECIST) criteria (responder). A confirmed CR requires 2 consecutive assessments of CR at least 28 days apart. A confirmed PR requires 2 consecutive assessments at least 28 days apart of PR or CR. All participants who did not meet the criteria for an objective response by the analysis cutoff date were considered non responders.
Safety Analysis Set: all participants who received at least 1 dose of trebananib and 1 dose of sunitinib. Participants with baseline measureable disease.

End point type	Secondary

End point timeframe:

48 months after last subject enrolled (LSE)

End point values	Trebananib 10 mg/kg + Sunitinib	Trebananib 15 mg/kg + Sunitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	41		
Units: percentage of participants				
number (confidence interval 80%)	58.1 (47.2 to 68.5)	63.4 (52.2 to 73.6)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

DOR was calculated as the time from the first confirmed objective response to first observed disease progression per modified RECIST v. 1.0 criteria or death due to any cause. DOR was calculated only for participants who had an objective response. Objective response was defined as either a confirmed CR or PR per modified RECIST criteria. A confirmed CR required 2 consecutive assessments of CR at least 28 days apart. A confirmed PR required 2 consecutive assessments at least 28 days apart of PR or CR. Participants not meeting criteria for progression by the analysis data cutoff date were censored at their last evaluable radiographical disease assessment date.
Safety Analysis Set: all participants who received at least 1 dose of trebananib and 1 dose of sunitinib. Participants with an objective response.

End point type	Secondary

End point timeframe:

48 months after LSE

End point values	Trebananib 10 mg/kg + Sunitinib	Trebananib 15 mg/kg + Sunitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	26		
Units: months				
median (confidence interval 80%)	18.0 (11.8 to 24.4)	18.4 (11.5 to 24.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR)

End point title	Disease Control Rate (DCR)

End point description:

DCR was defined as the percentage of participants with confirmed CR or PR or stable disease (SD), as defined by modified RECIST v1.0 criteria. A confirmed CR required 2 consecutive assessments of CR at least 28 days apart. A confirmed PR requires 2 consecutive assessments at least 28 days apart of PR or CR. CR or PR was confirmed at least 28 days after the criteria for response were first met. A response assessment of PR or CR that was not subsequently confirmed at least 4 weeks later were included as SD.

End point type	Secondary

End point timeframe:

48 months after LSE

End point values	Trebananib 10 mg/kg + Sunitinib	Trebananib 15 mg/kg + Sunitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	41		
Units: percentage of participants				
number (confidence interval 80%)	72.1 (61.5 to 81.0)	75.6 (64.9 to 84.3)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

PFS was defined as the time from enrollment date to date of disease progression (ie, radiographic progression) per modified RECIST v 1.0 criteria or death. Radiological imaging to assess disease status was performed until participants developed disease progression. Events of radiographic progression per modified RECIST 1.0 that occurred after initiation of subsequent anticancer therapy were not considered PFS events. Deaths occurring after initiation of subsequent anticancer therapy were considered PFS events. Participants not meeting criteria for progression by the analysis data cutoff date were censored at their last evaluable disease assessment date.
Safety Analysis Set: all participants who received at least 1 dose of trebananib and 1 dose of sunitinib.

End point type	Secondary

End point timeframe:

48 months after LSE

End point values	Trebananib 10 mg/kg + Sunitinib	Trebananib 15 mg/kg + Sunitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	42		
Units: months				
median (confidence interval 80%)	13.9 (11.0 to 16.1)	16.5 (13.3 to 21.4)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The time from enrollment date to date of death. Participants who had not died by the analysis data cutoff date were censored at their last contact date.
Safety Analysis Set: all participants who received at least 1 dose of trebananib and 1 dose of sunitinib.

End point type	Secondary

End point timeframe:

48 months after LSE

End point values	Trebananib 10 mg/kg + Sunitinib	Trebananib 15 mg/kg + Sunitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	42		
Units: months				
median (confidence interval 80%)	36.0 (26.0 to 52.9)	38.7 (31.5 to 42.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Percent Reduction From Baseline in the Sum of the Longest Diameters (SLD) of Target Lesions From Baseline to Post-Baseline Nadir

End point title	Maximum Percent Reduction From Baseline in the Sum of the Longest Diameters (SLD) of Target Lesions From Baseline to Post-Baseline Nadir

End point description:

Change in tumor burden was evaluated by the maximum percent reduction from baseline in the SLD of target lesions.
Safety Analysis Set: all participants who received at least 1 dose of trebananib and 1 dose of sunitinib. Participants with baseline measureable disease and non-missing baseline and post-baseline data.

End point type	Secondary

End point timeframe:

Baseline, 48 months after LSE

End point values	Trebananib 10 mg/kg + Sunitinib	Trebananib 15 mg/kg + Sunitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	40		
Units: percent reduction in SLD				
arithmetic mean (confidence interval 80%)	-36.0 (-43.4 to -28.6)	-41.8 (-48.4 to -35.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic Parameter: Maximum Observed Concentration (Cmax) for Trebananib Over Time

End point title	Pharmacokinetic Parameter: Maximum Observed Concentration (Cmax) for Trebananib Over Time

End point description:

Pharmacokinetics Analysis Set: participants with evaluable concentration data.

End point type	Secondary

End point timeframe:

Pre-infusion and up to 10 minutes post-infusion on Weeks 1, 4, 7, 10, 13, 22, 34, 46, 58, 70, 82, 94, 106, and safety follow-up (30 ±7 days after the last dose of study drug)

End point values	Trebananib 10 mg/kg + Sunitinib	Trebananib 15 mg/kg + Sunitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38[5]	41[6]		
Units: µg/mL				
median (full range (min-max))				
Week 1; n=38, 41	222 (63.2 to 819)	297 (152 to 535)		
Week 4; n=32, 22	285 (82.4 to 574)	377 (258 to 647)		
Week 7; n=32, 28	260 (75.3 to 550)	377 (238 to 1830)		
Week 10; n=32, 23	257 (105 to 630)	476 (184 to 770)		
Week 13; n=26, 22	219 (105 to 390)	385 (216 to 785)		
Week 22; n=31, 23	249 (92.8 to 385)	417 (224 to 758)		
Week 34; n=24, 18	240 (137 to 628)	387 (77.7 to 571)		
Week 46; n=19, 7	221 (159 to 700)	349 (235 to 908)		
Week 58; n=13, 0	229 (158 to 606)	99999 (99999 to 99999)		
Week 70; n=15, 0	185 (108 to 362)	99999 (99999 to 99999)		
Week 82; n=15, 0	223 (94.1 to 272)	99999 (99999 to 99999)		
Week 94; n=2, 0	270 (173 to 367)	99999 (99999 to 99999)		
Week 106; n=1, 0	289 (289 to 289)	99999 (99999 to 99999)		
Safety Follow-Up; n=11, 3	3.46 (1.26 to 6.16)	8.26 (5.62 to 11.8)		

Notes:

[5] - n=participants with an assessment at given time point.

[6] - n=participants with an assessment at given time point. 99999=not applicable (NA; n=0)

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic Parameter: Minimum Observed Concentration (Cmin) for Trebananib Over Time

End point title	Pharmacokinetic Parameter: Minimum Observed Concentration (Cmin) for Trebananib Over Time

End point description:

Pharmacokinetics Analysis Set: participants with evaluable concentration data.

End point type	Secondary

End point timeframe:

Pre-infusion on Weeks 4, 7, 10, 13, 22, 34, 46, 58, 70, 82, 94, 106, and safety follow-up (30 ±7 days after the last dose of study drug)

End point values	Trebananib 10 mg/kg + Sunitinib	Trebananib 15 mg/kg + Sunitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38[7]	29[8]		
Units: µg/mL				
median (full range (min-max))				
Week 4; n=38, 29	20.4 (6.22 to 41.9)	27.3 (6.35 to 95.4)		
Week 7; n=35, 29	30.1 (12.2 to 75.9)	42.0 (14.9 to 90.4)		
Week 10; n=33, 23	23.3 (9.09 to 72.3)	32.2 (13.9 to 85.6)		
Week 13; n=33, 25	26.1 (8.54 to 73.8)	43.2 (15.1 to 99.5)		
Week 22; n=32, 24	19.9 (8.59 to 63.1)	46.2 (16.2 to 73.7)		
Week 34; n=23, 18	24.1 (9.88 to 66.2)	35.9 (15.3 to 79.2)		
Week 46; n=21, 8	23.2 (6.46 to 64.4)	30.5 (21.0 to 71.8)		
Week 58; n=15, 0	27.9 (8.61 to 43.3)	99999 (99999 to 99999)		
Week 70; n=15, 0	26.2 (10.5 to 35.9)	99999 (99999 to 99999)		
Week 82; n=5, 0	22.5 (17.9 to 33.0)	99999 (99999 to 99999)		
Week 94; n=2, 0	25.9 (19.9 to 31.8)	99999 (99999 to 99999)		
Week 106; n=1, 0	19.3 (19.3 to 19.3)	99999 (99999 to 99999)		
Safety Follow-Up; n=11, 3	3.46 (1.26 to 6.16)	8.26 (5.62 to 11.8)		

Notes:

[7] - n=participants with an assessment at given time point.

[8] - n=participants with an assessment at given time point. 99999=not applicable (n=0)

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic Parameter: Cmin for Sunitinib Over Time

End point title	Pharmacokinetic Parameter: Cmin for Sunitinib Over Time

End point description:

Pharmacokinetics Analysis Set: participants with evaluable concentration data.

End point type	Secondary

End point timeframe:

Pre-infusion on Weeks 4, 7, 10, 16, 22, 34, 46, 58, 70, 82, 94, 106, and safety follow-up (30 ±7 days after the last dose of study drug)

End point values	Trebananib 10 mg/kg + Sunitinib	Trebananib 15 mg/kg + Sunitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9[9]	7[10]		
Units: ng/mL				
median (full range (min-max))				
Week 4; n=6, 6	58.6 (41.1 to 124)	70.6 (50.8 to 105)		
Week 7; n=9, 7	0.763 (-99999 to 4.68)	1.65 (-99999 to 3.78)		
Week 10; n=9, 5	66.1 (46.7 to 136)	64.7 (42.4 to 95.4)		
Week 16; n=5, 3	65.8 (47.1 to 91.9)	73.1 (49.1 to 92.7)		
Week 22; n=5, 1	49.0 (33.3 to 97.1)	41.2 (41.2 to 41.2)		
Week 34; n=4, 1	50.2 (-99999 to 110)	34.8 (34.8 to 34.8)		
Week 46; n=3, 2	59.5 (49.4 to 66.4)	33.5 (23.3 to 43.7)		
Week 58; n=2, 0	87.0 (51.9 to 122)	99999 (99999 to 99999)		
Week 70; n=1, 0	56.4 (56.4 to 56.4)	99999 (99999 to 99999)		
Week 82; n=1, 0	65.9 (65.9 to 65.9)	99999 (99999 to 99999)		
Week 94; n=1, 0	64.2 (64.2 to 64.2)	99999 (99999 to 99999)		
Week 106; n=1, 0	83.5 (83.5 to 83.5)	99999 (99999 to 99999)		
Safety Follow-Up; n=6, 0	-99999 (-99999 to 2.14)	99999 (99999 to 99999)		

Notes:

[9] - n=participants with assessment at given time point. -99999: < lower limit of quantification (LLOQ)

[10] - n=participants with assessment at given time point. 99999: NA (n=0); -99999: < LLOQ

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic Parameter: Cmin for Sunitinib Metabolite Over Time

End point title	Pharmacokinetic Parameter: Cmin for Sunitinib Metabolite Over Time

End point description:

Pharmacokinetics Analysis Set: participants with evaluable concentration data.

End point type	Secondary

End point timeframe:

Pre-infusion on Weeks 4, 7, 10, 16, 22, 34, 46, 58, 70, 82, 94, 106, and safety follow-up (30 ±7 days after the last dose of study drug)

End point values	Trebananib 10 mg/kg + Sunitinib	Trebananib 15 mg/kg + Sunitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9[11]	7[12]		
Units: ng/mL				
median (full range (min-max))				
Week 4; n=6, 6	22.8 (11.6 to 29.4)	29.2 (16.5 to 43.4)		
Week 7; n=9, 7	1.21 (0.582 to 3.89)	1.71 (0.405 to 3.22)		
Week 10; n=9, 5	19.2 (14.0 to 40.6)	21.5 (18.0 to 41.3)		
Week 16; n=5, 3	19.3 (13.7 to 22.7)	22.0 (21.6 to 40.5)		
Week 22; n=5, 1	12.7 (10.1 to 28.5)	18.7 (18.7 to 18.7)		
Week 34; n=4, 1	18.3 (-99999 to 38.3)	15.0 (15.0 to 15.0)		
Week 46; n=3, 2	15.0 (10.3 to 23.1)	10.6 (7.87 to 13.4)		
Week 58; n=2, 0	25.7 (20.1 to 31.2)	99999 (99999 to 99999)		
Week 70; n=1, 0	22.4 (22.4 to 22.4)	99999 (99999 to 99999)		
Week 82; n=1, 0	25.4 (25.4 to 25.4)	99999 (99999 to 99999)		
Week 94; n=1, 0	22.1 (22.1 to 22.1)	99999 (99999 to 99999)		
Week 106; n=1, 0	32.4 (32.4 to 32.4)	99999 (99999 to 99999)		
Safety Follow-Up; n=6, 0	0.138 (-99999 to 1.15)	99999 (99999 to 99999)		

Notes:

[11] - n=participants with assessment at given time point. -99999: < LLOQ

[12] - n=participants with assessment at given time point.99999=NA (n=0); -99999: < LLOQ

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Binding Antibody- or Neutralizing Antibody-Positive Post-Baseline

End point title	Number of Participants Binding Antibody- or Neutralizing Antibody-Positive Post-Baseline

End point description:

Transient positive results were defined as a positive post-baseline result followed by a negative result at the participant's last time point tested within the study period.
Safety Analysis Set: all participants who received at least 1 dose of trebananib and 1 dose of sunitinib.
Participants with a post-baseline result and a negative result or no result at baseline.

End point type	Secondary

End point timeframe:

48 months after LSE

End point values	Trebananib 10 mg/kg + Sunitinib	Trebananib 15 mg/kg + Sunitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	41		
Units: participants				
Binding Antibody Positive Post-Baseline (PBL)	0	0		
Binding Antibody Positive PBL, Transient	0	0		
Neutralizing Antibody Positive PBL	0	0		
Neutralizing Antibody Positive PBL, Transient	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 to 30 days after last dose. Median treatment duration of trebananib and sunitinib was 316 and 315 days, respectively, for Trebananib 10 mg/kg+Sunitinib, and 393 and 358 days, respectively, for Trebananib 15 mg/kg+Sunitinib.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Trebananib 10 mg/kg + Sunitinib

Reporting group description:

Trebananib 10 mg/kg IV QW plus sunitinib 50 mg PO QD 4 weeks on/2 weeks off

Reporting group title	Trebananib 15 mg/kg + Sunitinib

Reporting group description:

Trebananib 15 mg/kg IV QW plus sunitinib 50 mg PO QD 4 weeks on/2 weeks off

Serious adverse events	Trebananib 10 mg/kg + Sunitinib	Trebananib 15 mg/kg + Sunitinib	
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 43 (39.53%)	26 / 42 (61.90%)	
number of deaths (all causes)	30	26	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Renal cancer			
subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal cell carcinoma			
subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			

subjects affected / exposed	2 / 43 (4.65%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 43 (0.00%)	3 / 42 (7.14%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest discomfort			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	1 / 43 (2.33%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	2 / 43 (4.65%)	2 / 42 (4.76%)	
occurrences causally related to treatment / all	1 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	2 / 43 (4.65%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion site inflammation			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	2 / 43 (4.65%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			

subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 43 (0.00%)	3 / 42 (7.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Swelling			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Dyspnoea			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pleural effusion			
subjects affected / exposed	1 / 43 (2.33%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device occlusion			
subjects affected / exposed	0 / 43 (0.00%)	2 / 42 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			

subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Brain hypoxia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine with aura			
subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Monoplegia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile bone marrow aplasia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Glaucoma			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papilloedema			
subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uveitis			
subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vision blurred			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 43 (4.65%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Colitis			
subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 43 (2.33%)	3 / 42 (7.14%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus paralytic			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectourethral fistula			

subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stenosis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	0 / 43 (0.00%)	2 / 42 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			

subjects affected / exposed	1 / 43 (2.33%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperbilirubinaemia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis of jaw			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Anal abscess			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			

subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 43 (2.33%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 43 (2.33%)	2 / 42 (4.76%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Trebananib 10 mg/kg + Sunitinib	Trebananib 15 mg/kg + Sunitinib	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 43 (100.00%)	42 / 42 (100.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	26 / 43 (60.47%)	23 / 42 (54.76%)	
occurrences (all)	61	60	
Hypotension			
subjects affected / exposed	3 / 43 (6.98%)	7 / 42 (16.67%)	
occurrences (all)	5	10	
Pallor			
subjects affected / exposed	1 / 43 (2.33%)	3 / 42 (7.14%)	
occurrences (all)	1	4	
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	16 / 43 (37.21%)	20 / 42 (47.62%)	
occurrences (all)	60	66	
Catheter site pain			
subjects affected / exposed	3 / 43 (6.98%)	0 / 42 (0.00%)	
occurrences (all)	3	0	
Chest pain			
subjects affected / exposed	1 / 43 (2.33%)	5 / 42 (11.90%)	
occurrences (all)	1	6	
Chills			
subjects affected / exposed	3 / 43 (6.98%)	6 / 42 (14.29%)	
occurrences (all)	3	6	
Face oedema			
subjects affected / exposed	15 / 43 (34.88%)	21 / 42 (50.00%)	
occurrences (all)	50	50	
Fatigue			
subjects affected / exposed	16 / 43 (37.21%)	14 / 42 (33.33%)	
occurrences (all)	40	50	
Generalised oedema			
subjects affected / exposed	4 / 43 (9.30%)	3 / 42 (7.14%)	
occurrences (all)	6	7	
Influenza like illness			
subjects affected / exposed	2 / 43 (4.65%)	3 / 42 (7.14%)	
occurrences (all)	7	3	
Localised oedema			
subjects affected / exposed	6 / 43 (13.95%)	3 / 42 (7.14%)	
occurrences (all)	8	3	
Malaise			
subjects affected / exposed	4 / 43 (9.30%)	1 / 42 (2.38%)	
occurrences (all)	11	1	
Mucosal dryness			
subjects affected / exposed	3 / 43 (6.98%)	0 / 42 (0.00%)	
occurrences (all)	3	0	
Mucosal inflammation			
subjects affected / exposed	22 / 43 (51.16%)	25 / 42 (59.52%)	
occurrences (all)	51	51	

Oedema peripheral			
subjects affected / exposed	24 / 43 (55.81%)	24 / 42 (57.14%)	
occurrences (all)	59	65	
Pyrexia			
subjects affected / exposed	4 / 43 (9.30%)	3 / 42 (7.14%)	
occurrences (all)	4	11	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	13 / 43 (30.23%)	12 / 42 (28.57%)	
occurrences (all)	29	17	
Dysphonia			
subjects affected / exposed	7 / 43 (16.28%)	2 / 42 (4.76%)	
occurrences (all)	8	2	
Dyspnoea			
subjects affected / exposed	7 / 43 (16.28%)	8 / 42 (19.05%)	
occurrences (all)	7	17	
Dyspnoea exertional			
subjects affected / exposed	3 / 43 (6.98%)	4 / 42 (9.52%)	
occurrences (all)	6	5	
Epistaxis			
subjects affected / exposed	12 / 43 (27.91%)	6 / 42 (14.29%)	
occurrences (all)	23	7	
Hiccups			
subjects affected / exposed	3 / 43 (6.98%)	1 / 42 (2.38%)	
occurrences (all)	4	1	
Nasal dryness			
subjects affected / exposed	3 / 43 (6.98%)	0 / 42 (0.00%)	
occurrences (all)	4	0	
Oropharyngeal pain			
subjects affected / exposed	7 / 43 (16.28%)	5 / 42 (11.90%)	
occurrences (all)	11	12	
Pleural effusion			
subjects affected / exposed	5 / 43 (11.63%)	3 / 42 (7.14%)	
occurrences (all)	7	4	
Rhinorrhoea			

subjects affected / exposed	3 / 43 (6.98%)	2 / 42 (4.76%)	
occurrences (all)	5	2	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 43 (9.30%)	2 / 42 (4.76%)	
occurrences (all)	5	2	
Depression			
subjects affected / exposed	4 / 43 (9.30%)	3 / 42 (7.14%)	
occurrences (all)	4	8	
Insomnia			
subjects affected / exposed	8 / 43 (18.60%)	5 / 42 (11.90%)	
occurrences (all)	11	5	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 43 (6.98%)	3 / 42 (7.14%)	
occurrences (all)	5	9	
Amylase increased			
subjects affected / exposed	1 / 43 (2.33%)	3 / 42 (7.14%)	
occurrences (all)	1	6	
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 43 (6.98%)	2 / 42 (4.76%)	
occurrences (all)	4	6	
Blood creatinine increased			
subjects affected / exposed	3 / 43 (6.98%)	3 / 42 (7.14%)	
occurrences (all)	3	4	
Lipase increased			
subjects affected / exposed	1 / 43 (2.33%)	5 / 42 (11.90%)	
occurrences (all)	1	6	
Weight decreased			
subjects affected / exposed	5 / 43 (11.63%)	4 / 42 (9.52%)	
occurrences (all)	8	11	
Weight increased			
subjects affected / exposed	4 / 43 (9.30%)	1 / 42 (2.38%)	
occurrences (all)	39	1	
Injury, poisoning and procedural complications			

Fall			
subjects affected / exposed	4 / 43 (9.30%)	0 / 42 (0.00%)	
occurrences (all)	5	0	
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	1 / 43 (2.33%)	3 / 42 (7.14%)	
occurrences (all)	1	3	
Nervous system disorders			
Ageusia			
subjects affected / exposed	5 / 43 (11.63%)	3 / 42 (7.14%)	
occurrences (all)	5	4	
Dizziness			
subjects affected / exposed	10 / 43 (23.26%)	6 / 42 (14.29%)	
occurrences (all)	11	21	
Dysgeusia			
subjects affected / exposed	6 / 43 (13.95%)	3 / 42 (7.14%)	
occurrences (all)	8	4	
Formication			
subjects affected / exposed	4 / 43 (9.30%)	1 / 42 (2.38%)	
occurrences (all)	5	1	
Headache			
subjects affected / exposed	13 / 43 (30.23%)	6 / 42 (14.29%)	
occurrences (all)	25	10	
Neuropathy peripheral			
subjects affected / exposed	3 / 43 (6.98%)	4 / 42 (9.52%)	
occurrences (all)	4	4	
Paraesthesia			
subjects affected / exposed	3 / 43 (6.98%)	3 / 42 (7.14%)	
occurrences (all)	4	4	
Presyncope			
subjects affected / exposed	4 / 43 (9.30%)	1 / 42 (2.38%)	
occurrences (all)	6	1	
Sciatica			
subjects affected / exposed	3 / 43 (6.98%)	1 / 42 (2.38%)	
occurrences (all)	3	1	
Syncope			

subjects affected / exposed	1 / 43 (2.33%)	3 / 42 (7.14%)	
occurrences (all)	4	3	
Taste disorder			
subjects affected / exposed	14 / 43 (32.56%)	10 / 42 (23.81%)	
occurrences (all)	26	17	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 43 (11.63%)	7 / 42 (16.67%)	
occurrences (all)	12	11	
Leukopenia			
subjects affected / exposed	2 / 43 (4.65%)	3 / 42 (7.14%)	
occurrences (all)	4	16	
Neutropenia			
subjects affected / exposed	5 / 43 (11.63%)	4 / 42 (9.52%)	
occurrences (all)	13	15	
Thrombocytopenia			
subjects affected / exposed	14 / 43 (32.56%)	11 / 42 (26.19%)	
occurrences (all)	23	23	
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	3 / 43 (6.98%)	1 / 42 (2.38%)	
occurrences (all)	3	1	
Tinnitus			
subjects affected / exposed	3 / 43 (6.98%)	0 / 42 (0.00%)	
occurrences (all)	3	0	
Vertigo			
subjects affected / exposed	1 / 43 (2.33%)	4 / 42 (9.52%)	
occurrences (all)	1	4	
Eye disorders			
Eyelid oedema			
subjects affected / exposed	10 / 43 (23.26%)	8 / 42 (19.05%)	
occurrences (all)	47	16	
Glaucoma			
subjects affected / exposed	3 / 43 (6.98%)	0 / 42 (0.00%)	
occurrences (all)	3	0	
Lacrimation increased			

subjects affected / exposed	13 / 43 (30.23%)	12 / 42 (28.57%)	
occurrences (all)	18	19	
Periorbital oedema			
subjects affected / exposed	5 / 43 (11.63%)	8 / 42 (19.05%)	
occurrences (all)	13	11	
Visual acuity reduced			
subjects affected / exposed	3 / 43 (6.98%)	0 / 42 (0.00%)	
occurrences (all)	3	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	3 / 43 (6.98%)	2 / 42 (4.76%)	
occurrences (all)	7	2	
Abdominal distension			
subjects affected / exposed	3 / 43 (6.98%)	0 / 42 (0.00%)	
occurrences (all)	3	0	
Abdominal pain			
subjects affected / exposed	13 / 43 (30.23%)	15 / 42 (35.71%)	
occurrences (all)	28	23	
Abdominal pain upper			
subjects affected / exposed	14 / 43 (32.56%)	9 / 42 (21.43%)	
occurrences (all)	33	12	
Aphthous ulcer			
subjects affected / exposed	9 / 43 (20.93%)	6 / 42 (14.29%)	
occurrences (all)	15	6	
Ascites			
subjects affected / exposed	4 / 43 (9.30%)	1 / 42 (2.38%)	
occurrences (all)	4	1	
Constipation			
subjects affected / exposed	13 / 43 (30.23%)	8 / 42 (19.05%)	
occurrences (all)	15	11	
Diarrhoea			
subjects affected / exposed	33 / 43 (76.74%)	32 / 42 (76.19%)	
occurrences (all)	144	112	
Dry mouth			
subjects affected / exposed	6 / 43 (13.95%)	3 / 42 (7.14%)	
occurrences (all)	9	3	

Dyspepsia			
subjects affected / exposed	16 / 43 (37.21%)	10 / 42 (23.81%)	
occurrences (all)	23	20	
Dysphagia			
subjects affected / exposed	1 / 43 (2.33%)	5 / 42 (11.90%)	
occurrences (all)	2	7	
Flatulence			
subjects affected / exposed	2 / 43 (4.65%)	5 / 42 (11.90%)	
occurrences (all)	2	5	
Gastrooesophageal reflux disease			
subjects affected / exposed	8 / 43 (18.60%)	3 / 42 (7.14%)	
occurrences (all)	9	5	
Gingival pain			
subjects affected / exposed	0 / 43 (0.00%)	3 / 42 (7.14%)	
occurrences (all)	0	3	
Haemorrhoids			
subjects affected / exposed	3 / 43 (6.98%)	5 / 42 (11.90%)	
occurrences (all)	4	21	
Nausea			
subjects affected / exposed	22 / 43 (51.16%)	19 / 42 (45.24%)	
occurrences (all)	61	48	
Oesophagitis			
subjects affected / exposed	1 / 43 (2.33%)	3 / 42 (7.14%)	
occurrences (all)	2	5	
Stomatitis			
subjects affected / exposed	4 / 43 (9.30%)	8 / 42 (19.05%)	
occurrences (all)	17	18	
Vomiting			
subjects affected / exposed	17 / 43 (39.53%)	13 / 42 (30.95%)	
occurrences (all)	51	24	
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 43 (2.33%)	3 / 42 (7.14%)	
occurrences (all)	1	9	
Skin and subcutaneous tissue disorders			

Dry skin				
subjects affected / exposed	18 / 43 (41.86%)	6 / 42 (14.29%)		
occurrences (all)	26	8		
Erythema				
subjects affected / exposed	6 / 43 (13.95%)	2 / 42 (4.76%)		
occurrences (all)	9	2		
Hair colour changes				
subjects affected / exposed	5 / 43 (11.63%)	3 / 42 (7.14%)		
occurrences (all)	6	3		
Hyperhidrosis				
subjects affected / exposed	3 / 43 (6.98%)	1 / 42 (2.38%)		
occurrences (all)	5	5		
Hyperkeratosis				
subjects affected / exposed	4 / 43 (9.30%)	4 / 42 (9.52%)		
occurrences (all)	5	5		
Nail disorder				
subjects affected / exposed	4 / 43 (9.30%)	1 / 42 (2.38%)		
occurrences (all)	4	1		
Palmar-plantar erythrodysaesthesia syndrome				
subjects affected / exposed	21 / 43 (48.84%)	18 / 42 (42.86%)		
occurrences (all)	91	45		
Pruritus				
subjects affected / exposed	5 / 43 (11.63%)	4 / 42 (9.52%)		
occurrences (all)	8	4		
Rash				
subjects affected / exposed	9 / 43 (20.93%)	9 / 42 (21.43%)		
occurrences (all)	15	18		
Skin discolouration				
subjects affected / exposed	4 / 43 (9.30%)	2 / 42 (4.76%)		
occurrences (all)	4	2		
Skin disorder				
subjects affected / exposed	3 / 43 (6.98%)	0 / 42 (0.00%)		
occurrences (all)	4	0		
Skin exfoliation				

subjects affected / exposed	4 / 43 (9.30%)	3 / 42 (7.14%)	
occurrences (all)	5	5	
Skin toxicity			
subjects affected / exposed	4 / 43 (9.30%)	4 / 42 (9.52%)	
occurrences (all)	41	20	
Yellow skin			
subjects affected / exposed	4 / 43 (9.30%)	5 / 42 (11.90%)	
occurrences (all)	4	5	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	3 / 43 (6.98%)	5 / 42 (11.90%)	
occurrences (all)	3	8	
Proteinuria			
subjects affected / exposed	2 / 43 (4.65%)	6 / 42 (14.29%)	
occurrences (all)	2	13	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	2 / 43 (4.65%)	5 / 42 (11.90%)	
occurrences (all)	2	7	
Hypothyroidism			
subjects affected / exposed	21 / 43 (48.84%)	18 / 42 (42.86%)	
occurrences (all)	25	24	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	17 / 43 (39.53%)	10 / 42 (23.81%)	
occurrences (all)	30	19	
Back pain			
subjects affected / exposed	12 / 43 (27.91%)	5 / 42 (11.90%)	
occurrences (all)	19	5	
Bone pain			
subjects affected / exposed	7 / 43 (16.28%)	4 / 42 (9.52%)	
occurrences (all)	8	4	
Groin pain			
subjects affected / exposed	3 / 43 (6.98%)	2 / 42 (4.76%)	
occurrences (all)	5	2	
Muscle spasms			

subjects affected / exposed	6 / 43 (13.95%)	4 / 42 (9.52%)	
occurrences (all)	12	4	
Muscular weakness			
subjects affected / exposed	4 / 43 (9.30%)	5 / 42 (11.90%)	
occurrences (all)	6	10	
Musculoskeletal pain			
subjects affected / exposed	7 / 43 (16.28%)	7 / 42 (16.67%)	
occurrences (all)	8	12	
Myalgia			
subjects affected / exposed	6 / 43 (13.95%)	6 / 42 (14.29%)	
occurrences (all)	7	7	
Pain in extremity			
subjects affected / exposed	10 / 43 (23.26%)	5 / 42 (11.90%)	
occurrences (all)	25	10	
Spinal pain			
subjects affected / exposed	3 / 43 (6.98%)	1 / 42 (2.38%)	
occurrences (all)	4	1	
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 43 (6.98%)	3 / 42 (7.14%)	
occurrences (all)	3	3	
Conjunctivitis			
subjects affected / exposed	4 / 43 (9.30%)	4 / 42 (9.52%)	
occurrences (all)	4	4	
Cystitis			
subjects affected / exposed	0 / 43 (0.00%)	3 / 42 (7.14%)	
occurrences (all)	0	3	
Ear infection			
subjects affected / exposed	1 / 43 (2.33%)	3 / 42 (7.14%)	
occurrences (all)	1	3	
Gastroenteritis			
subjects affected / exposed	6 / 43 (13.95%)	1 / 42 (2.38%)	
occurrences (all)	6	1	
Influenza			
subjects affected / exposed	4 / 43 (9.30%)	1 / 42 (2.38%)	
occurrences (all)	4	1	

Laryngitis			
subjects affected / exposed	2 / 43 (4.65%)	3 / 42 (7.14%)	
occurrences (all)	2	3	
Nasopharyngitis			
subjects affected / exposed	4 / 43 (9.30%)	2 / 42 (4.76%)	
occurrences (all)	4	3	
Oral herpes			
subjects affected / exposed	3 / 43 (6.98%)	2 / 42 (4.76%)	
occurrences (all)	3	2	
Pharyngitis			
subjects affected / exposed	0 / 43 (0.00%)	3 / 42 (7.14%)	
occurrences (all)	0	4	
Rhinitis			
subjects affected / exposed	8 / 43 (18.60%)	4 / 42 (9.52%)	
occurrences (all)	17	6	
Sinusitis			
subjects affected / exposed	2 / 43 (4.65%)	3 / 42 (7.14%)	
occurrences (all)	2	3	
Tooth abscess			
subjects affected / exposed	5 / 43 (11.63%)	2 / 42 (4.76%)	
occurrences (all)	5	2	
Upper respiratory tract infection			
subjects affected / exposed	5 / 43 (11.63%)	7 / 42 (16.67%)	
occurrences (all)	8	9	
Urinary tract infection			
subjects affected / exposed	1 / 43 (2.33%)	4 / 42 (9.52%)	
occurrences (all)	1	5	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	17 / 43 (39.53%)	24 / 42 (57.14%)	
occurrences (all)	47	44	
Dehydration			
subjects affected / exposed	5 / 43 (11.63%)	3 / 42 (7.14%)	
occurrences (all)	6	8	
Hyperglycaemia			

subjects affected / exposed	0 / 43 (0.00%)	3 / 42 (7.14%)	
occurrences (all)	0	4	
Hypoalbuminaemia			
subjects affected / exposed	1 / 43 (2.33%)	3 / 42 (7.14%)	
occurrences (all)	2	3	
Hypokalaemia			
subjects affected / exposed	4 / 43 (9.30%)	3 / 42 (7.14%)	
occurrences (all)	10	6	
Hypophosphataemia			
subjects affected / exposed	3 / 43 (6.98%)	8 / 42 (19.05%)	
occurrences (all)	3	16	
Obesity			
subjects affected / exposed	0 / 43 (0.00%)	3 / 42 (7.14%)	
occurrences (all)	0	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 December 2009	- Cohort B (trebananib 15 mg/kg IV QW plus sunitinib 50 mg PO QD given 4 weeks on/2 weeks off) was added. - The enrollment period was extended to 10 months to facilitate the enrollment of an additional 40 subjects.
21 June 2011	- Pleural effusion and ascites are known identified risks of trebananib, and thus a new toxicity management section was added to provide guidance to participating investigators of the study. - Toxicity management for thromboembolic events, hypokalemia, and grade 3 toxicities was clarified. - The radiologic scanning frequency interval after 3 years on study was reduced to every 6 months. - Guidelines for proscribed medications were added including immune modulators, CYP3A4 strong inducers and inhibitors, and amiodarone as excluded medications during the study. The use of low dose warfarin (≤ 1 mg PO QD) or low molecular weight heparin for prophylaxis against thrombosis was disallowed. - The Cox regression model estimation of PFS hazard rate was removed.
24 November 2012	- Serious adverse events occurring after conclusion of the study AND thought to be possibly related to investigational product were to be collected and recorded in the subject's medical record, and reported to Amgen within 1 working day of discovery or notification of the event. - The process for determination of expectedness of clinical trial adverse events for the purpose of expedited reporting to regulatory agencies globally was amended. - The Pregnancy and Lactation Reporting section was updated, and a new lactation notification worksheet was added

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported