Clinical trial results:
AN OPEN-LABEL SUNITINIB MALATE (SU011248) CONTINUATION PROTOCOL FOR PATIENTS WHO HAVE COMPLETED A PRIOR SUNITINIB STUDY AND ARE JUDGED BY THE INVESTIGATOR TO HAVE THE POTENTIAL TO BENEFIT FROM SUNITINIB TREATMENT

Summary

EudraCT number	2006-006538-16
Trial protocol	DE BE FR DK GB NL BG ES
Global end of trial date	12 September 2014

Results information

Result version number	v1 (current)
This version publication date	05 April 2016
First version publication date	14 August 2015

Trial information

Trial identification

Sponsor protocol code	A6181114

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00428220
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 East 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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	17 February 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 September 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To provide access to sunitinib treatment for subjects who had participated in previous "parent" or extension sunitinib protocols and who had the potential as judged by the investigator to derive clinical benefit from sunitinib treatment.
• To assess the long-term safety and tolerability of sunitinib.
• To assess the duration of clinical benefit for subjects taking sunitinib.

Protection of trial subjects:

This study was designed and monitored in accordance with Pfizer's and the contract research organization's standard operating procedures (SOPs), which comply with the ethical principles of Good Clinical Practice (GCP) as required by the major regulatory authorities, and in accordance with the Declaration of Helsinki. Pfizer Compliance Oversight Leads (COLs) provided study and site level oversight to ensure that the study was delivered to high quality standards. COLs performed on-site and remote oversight to assess monitoring effectiveness and ensure compliance with the study protocol by investigational sites according to ICH-GCP, applicable SOPs, and local regulations.

Background therapy:

This was an open-label continuation or extension protocol. The protocol permitted continued access to sunitinib for participants who had participated in a previous parent or extension sunitinib study and who had been judged by the investigator to have had the potential to derive clinical benefit from continuing sunitinib dosing.

Evidence for comparator: -

Actual start date of recruitment	13 July 2007
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	Brazil: 13
Country: Number of subjects enrolled	Canada: 12
Country: Number of subjects enrolled	Colombia: 3
Country: Number of subjects enrolled	Hong Kong: 10
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 22
Country: Number of subjects enrolled	Mexico: 10
Country: Number of subjects enrolled	Philippines: 1
Country: Number of subjects enrolled	Singapore: 4
Country: Number of subjects enrolled	Taiwan: 18
Country: Number of subjects enrolled	United States: 14
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	United Kingdom: 11

Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	France: 49
Country: Number of subjects enrolled	Germany: 17
Country: Number of subjects enrolled	Argentina: 9
Country: Number of subjects enrolled	Australia: 12
Worldwide total number of subjects	223
EEA total number of subjects	95

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)	169
From 65 to 84 years	54
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In this open-label extension study, access to sunitinib was provided to participants who had participated in a previous parent study and who had been judged by the investigator to have likely clinical benefit from continuing sunitinib dosing.

Pre-assignment

Screening details:

Participants receiving sunitinib in previous studies began treatment in this study with the last dose they were taking in the parent or extension study. Participants were to continue to access sunitinib on this protocol as long as there was evidence of disease control and/or clinical benefit in the judgment of the investigator.

Pre-assignment period milestones

Number of subjects started	226[1]
Number of subjects completed	223

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Long-time follow-up of previous study: 3

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Of the 226 participants screened, 3 participants were not treated since they were only in long-time follow-up of their parent study. Hence, 223 participants were treated and received at least 1 dose of study drug.

Period 1

Period 1 title	Sunitinib (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Sunitinib

Arm description:

Participants receiving treatment on single-agent sunitinib on continuous dosing regimens returned for study visits at Day 28, and every 8 weeks thereafter. Participants on regimens other than single-agent sunitinib on continuous dosing followed the schedule of activities from their parent or extension protocol. Sunitinib-naïve participants (ie, those not treated with sunitinib in the previous parent study) received a starting dose of 37.5 mg sunitinib once daily.

Arm type	Experimental
Investigational medicinal product name	Sunitinib malate
Investigational medicinal product code	SU011248
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

All participants received open-label sunitinib and took orally without regard to meals beginning on Day 1 of the study. Participants receiving treatment on single-agent sunitinib on continuous dosing regimens returned for study visits at Day 28, and every 8 weeks thereafter. Participants on regimens other than single-agent sunitinib on continuous dosing followed the schedule of activities from their parent or extension protocol. Sunitinib-naïve participants (ie, those not treated with sunitinib in the previous parent study) received a starting dose of 37.5 mg sunitinib once daily.

Number of subjects in period 1	Sunitinib
Started	223
Completed	0
Not completed	223
Global deterioration of health status	7
Adverse event, non-fatal	51
Participant died	8
Participant refused continued treatment	7
Other reasons	23
Lost to follow-up	4
Objective progression or relapse	123

Baseline characteristics

Reporting groups	
Reporting group title	Sunitinib

Reporting group description:

Participants receiving treatment on single-agent sunitinib on continuous dosing regimens returned for study visits at Day 28, and every 8 weeks thereafter. Participants on regimens other than single-agent sunitinib on continuous dosing followed the schedule of activities from their parent or extension protocol. Sunitinib-naïve participants (ie, those not treated with sunitinib in the previous parent study) received a starting dose of 37.5 mg sunitinib once daily.

Reporting group values	Sunitinib	Total	
Number of subjects	223	223	
Age categorical			
Units: Subjects			
Adults (18-64 years)	169	169	
From 65-84 years	54	54	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	55.2		
standard deviation	± 12.5	-	
Gender categorical			
Demographic data is presented in safety population set. The safety population was defined as all participants enrolled in the study who received at least one dose of study drug in this study.			
Units: Subjects			
Female	130	130	
Male	93	93	

End points

End points reporting groups

Reporting group title	Sunitinib

Reporting group description:

Participants receiving treatment on single-agent sunitinib on continuous dosing regimens returned for study visits at Day 28, and every 8 weeks thereafter. Participants on regimens other than single-agent sunitinib on continuous dosing followed the schedule of activities from their parent or extension protocol. Sunitinib-naïve participants (ie, those not treated with sunitinib in the previous parent study) received a starting dose of 37.5 mg sunitinib once daily.

Primary: Number of Participants With Treatment-emergent (All Causalities) - Safety Population

End point title	Number of Participants With Treatment-emergent (All Causalities) - Safety Population[1]

End point description:

Assessment of adverse events (AEs) included type, incidence, severity (graded by the National Cancer Institute [NCI] Common Terminology Criteria for Adverse Events [CTCAE], Version 3.0, timing, seriousness, and relatedness; and laboratory abnormalities. The safety population was defined as all participants enrolled in the study who received at least one dose of study drug in this study.

End point type	Primary

End point timeframe:

From first day of treatment on the current study up to 28 days post the last dose of study treatment

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis provided for Number of Participants With Treatment-emergent Adverse Events (AEs) (All Causalities)

End point values	Sunitinib			
Subject group type	Reporting group			
Number of subjects analysed	223			
Units: participants				
Participants with AEs	221			
Participants with serious adverse events (SAE)	90			
Participants with grade 3 or 4 AEs	174			
Participants with grade 5 AEs	24			
Participants discontinued due to AEs	67			
Participants with dose reduction due to AEs	66			
Temporary discontinuations due to AEs	146			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Treatment-emergent AEs (Treatment-Related)

End point title	Number of Participants With Treatment-emergent AEs

	(Treatment-Related)[2]

End point description:

Assessment of AEs included type, incidence, severity (graded by the NCI CTCAE, Version 3.0), timing, seriousness, and relatedness; and laboratory abnormalities.

End point type	Primary

End point timeframe:

From first day of treatment on the current study up to 28 days post the last dose of study treatment

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis provided for Number of Participants With Treatment-emergent AEs (Treatment-Related)

End point values	Sunitinib			
Subject group type	Reporting group			
Number of subjects analysed	223			
Units: participants				
Participants with AE	217			
Participants with SAE	39			
Participants with grade 3 or 4 AEs	146			
Participants with grade 5 AEs	0			
Participants discontinued due to AEs	29			
Participants with dose reduction due to AEs	64			
Temporary discontinuations due to AEs	135			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Summary of Duration of Clinical Benefit

End point title	Summary of Duration of Clinical Benefit

End point description:

The mean duration of clinical benefit summarized by parent studies ranged from 22.1 weeks (range 0.6 to 128.3 weeks) in parent study A6181107 (69 participants) to 227.5 weeks (range 186.6 to 268.4 weeks) in parent study A6181170 (2 participants).

End point type	Other pre-specified

End point timeframe:

From the first day of treatment on the parent protocol until the end of sunitinib treatment in this study for sunitinib treated participants. Length of time in this study for participants on placebo or comparator drug.

End point values	Sunitinib			
Subject group type	Reporting group			
Number of subjects analysed	223			
Units: Weeks	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first day of treatment on the current study up to 28 days post the last dose of study treatment

Adverse event reporting additional description:

The same event may appear as both an AE and a SAE. However, what is presented are distinct events. An event may be categorized as serious in one participant and as nonserious in another participant, or one participant may have experienced both a serious and nonserious event during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Sunitinib

Reporting group description:

Participants receiving treatment on single-agent sunitinib on continuous dosing regimens returned for study visits at Day 28, and every 8 weeks thereafter. Participants on regimens other than single-agent sunitinib on continuous dosing followed the schedule of activities from their parent or extension protocol. Sunitinib-naïve participants (ie, those not treated with sunitinib in the previous parent study) received a starting dose of 37.5 mg sunitinib once daily

Serious adverse events	Sunitinib		
Total subjects affected by serious adverse events			
subjects affected / exposed	90 / 223 (40.36%)		
number of deaths (all causes)	111		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Breast cancer			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 3		
Chronic myeloid leukaemia			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Infected neoplasm				
subjects affected / exposed	1 / 223 (0.45%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lymphangiosis carcinomatosa				
subjects affected / exposed	1 / 223 (0.45%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	1 / 223 (0.45%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tumour haemorrhage				
subjects affected / exposed	1 / 223 (0.45%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Hypertension				
subjects affected / exposed	1 / 223 (0.45%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pelvic venous thrombosis				
subjects affected / exposed	1 / 223 (0.45%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Thrombosis				
subjects affected / exposed	1 / 223 (0.45%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Venous thrombosis limb				
subjects affected / exposed	1 / 223 (0.45%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Aortic dissection				

subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 223 (1.35%)		
occurrences causally related to treatment / all	5 / 5		
deaths causally related to treatment / all	0 / 0		
Chest pain			
subjects affected / exposed	2 / 223 (0.90%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Disease progression			
subjects affected / exposed	12 / 223 (5.38%)		
occurrences causally related to treatment / all	0 / 18		
deaths causally related to treatment / all	0 / 18		
Fatigue			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Gait disturbance			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			
subjects affected / exposed	5 / 223 (2.24%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	0 / 1		
Generalised oedema			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mucosal inflammation			

subjects affected / exposed	1 / 223 (0.45%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oedema				
subjects affected / exposed	1 / 223 (0.45%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	5 / 223 (2.24%)			
occurrences causally related to treatment / all	2 / 5			
deaths causally related to treatment / all	0 / 0			
Sudden death				
subjects affected / exposed	1 / 223 (0.45%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Reproductive system and breast disorders				
Scrotal erythema				
subjects affected / exposed	1 / 223 (0.45%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Cough				
subjects affected / exposed	1 / 223 (0.45%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	3 / 223 (1.35%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Epistaxis				
subjects affected / exposed	2 / 223 (0.90%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			

Lung disorder				
subjects affected / exposed	1 / 223 (0.45%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	1 / 223 (0.45%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	2 / 223 (0.90%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	2 / 223 (0.90%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	1 / 223 (0.45%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Confusional state				
subjects affected / exposed	1 / 223 (0.45%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Depression				
subjects affected / exposed	1 / 223 (0.45%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mental status changes				
subjects affected / exposed	1 / 223 (0.45%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Suicide attempt				

subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood calcium increased			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ejection fraction decreased			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Weight decreased			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Lipase increased			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Joint dislocation			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pelvic fracture			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Road traffic accident			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Ulna fracture			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Acute myocardial infarction			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
Convulsion			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Encephalopathy			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatic encephalopathy			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		

Lethargy			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolic encephalopathy			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 223 (2.24%)		
occurrences causally related to treatment / all	5 / 5		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	8 / 223 (3.59%)		
occurrences causally related to treatment / all	1 / 15		
deaths causally related to treatment / all	0 / 0		
Abdominal pain upper			
subjects affected / exposed	2 / 223 (0.90%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		

Ascites			
subjects affected / exposed	2 / 223 (0.90%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Diarrhoea			
subjects affected / exposed	6 / 223 (2.69%)		
occurrences causally related to treatment / all	6 / 8		
deaths causally related to treatment / all	0 / 0		
Duodenitis			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	2 / 223 (0.90%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Haematemesis			
subjects affected / exposed	2 / 223 (0.90%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal perforation			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Mallory-Weiss syndrome			

subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	3 / 223 (1.35%)		
occurrences causally related to treatment / all	5 / 5		
deaths causally related to treatment / all	0 / 0		
Oesophagitis			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	2 / 223 (0.90%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Peritoneal haemorrhage			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumatosis intestinalis			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subileus			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			

subjects affected / exposed	7 / 223 (3.14%)		
occurrences causally related to treatment / all	6 / 14		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholangitis			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystitis acute			
subjects affected / exposed	2 / 223 (0.90%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Hepatic failure			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Jaundice			
subjects affected / exposed	2 / 223 (0.90%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Jaundice cholestatic			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin exfoliation			

subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure acute			
subjects affected / exposed	2 / 223 (0.90%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 223 (1.79%)		
occurrences causally related to treatment / all	2 / 5		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	3 / 223 (1.35%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Flank pain			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc protrusion			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteonecrosis of jaw			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Pain in extremity			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lymphangitis			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	2 / 223 (0.90%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumonia bacterial			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Urinary tract infection			
subjects affected / exposed	2 / 223 (0.90%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Urosepsis			

subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Decreased appetite			
subjects affected / exposed	3 / 223 (1.35%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	2 / 223 (0.90%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	1 / 223 (0.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Sunitinib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	219 / 223 (98.21%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	64 / 223 (28.70%)		
occurrences (all)	99		
General disorders and administration			

site conditions			
Asthenia			
subjects affected / exposed	67 / 223 (30.04%)		
occurrences (all)	171		
Chest pain			
subjects affected / exposed	14 / 223 (6.28%)		
occurrences (all)	16		
Face oedema			
subjects affected / exposed	17 / 223 (7.62%)		
occurrences (all)	25		
Fatigue			
subjects affected / exposed	83 / 223 (37.22%)		
occurrences (all)	194		
Mucosal inflammation			
subjects affected / exposed	58 / 223 (26.01%)		
occurrences (all)	109		
Oedema peripheral			
subjects affected / exposed	30 / 223 (13.45%)		
occurrences (all)	37		
Pain			
subjects affected / exposed	13 / 223 (5.83%)		
occurrences (all)	14		
Pyrexia			
subjects affected / exposed	26 / 223 (11.66%)		
occurrences (all)	33		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	35 / 223 (15.70%)		
occurrences (all)	48		
Dyspnoea			
subjects affected / exposed	44 / 223 (19.73%)		
occurrences (all)	68		
Epistaxis			
subjects affected / exposed	43 / 223 (19.28%)		
occurrences (all)	79		
Oropharyngeal pain			

subjects affected / exposed	19 / 223 (8.52%)		
occurrences (all)	26		
Pleural effusion			
subjects affected / exposed	14 / 223 (6.28%)		
occurrences (all)	16		
Psychiatric disorders			
Depression			
subjects affected / exposed	14 / 223 (6.28%)		
occurrences (all)	22		
Insomnia			
subjects affected / exposed	35 / 223 (15.70%)		
occurrences (all)	40		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	21 / 223 (9.42%)		
occurrences (all)	31		
Aspartate aminotransferase increased			
subjects affected / exposed	15 / 223 (6.73%)		
occurrences (all)	28		
Blood creatinine increased			
subjects affected / exposed	13 / 223 (5.83%)		
occurrences (all)	22		
Haemoglobin decreased			
subjects affected / exposed	20 / 223 (8.97%)		
occurrences (all)	45		
Neutrophil count decreased			
subjects affected / exposed	16 / 223 (7.17%)		
occurrences (all)	86		
Platelet count decreased			
subjects affected / exposed	19 / 223 (8.52%)		
occurrences (all)	38		
Weight decreased			
subjects affected / exposed	36 / 223 (16.14%)		
occurrences (all)	57		
Nervous system disorders			

Dizziness subjects affected / exposed occurrences (all)	16 / 223 (7.17%) 18		
Dysgeusia subjects affected / exposed occurrences (all)	60 / 223 (26.91%) 86		
Headache subjects affected / exposed occurrences (all)	44 / 223 (19.73%) 70		
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	41 / 223 (18.39%) 100		
Leukopenia subjects affected / exposed occurrences (all)	35 / 223 (15.70%) 106		
Neutropenia subjects affected / exposed occurrences (all)	76 / 223 (34.08%) 358		
Thrombocytopenia subjects affected / exposed occurrences (all)	57 / 223 (25.56%) 153		
Eye disorders			
Lacrimation increased subjects affected / exposed occurrences (all)	13 / 223 (5.83%) 17		
Gastrointestinal disorders			
Abdominal distension subjects affected / exposed occurrences (all)	20 / 223 (8.97%) 28		
abdominal pain subjects affected / exposed occurrences (all)	62 / 223 (27.80%) 121		
Abdominal pain upper subjects affected / exposed occurrences (all)	46 / 223 (20.63%) 73		
Constipation			

subjects affected / exposed	41 / 223 (18.39%)		
occurrences (all)	50		
Diarrhoea			
subjects affected / exposed	142 / 223 (63.68%)		
occurrences (all)	438		
Dry mouth			
subjects affected / exposed	14 / 223 (6.28%)		
occurrences (all)	17		
Dyspepsia			
subjects affected / exposed	36 / 223 (16.14%)		
occurrences (all)	57		
Gastritis			
subjects affected / exposed	13 / 223 (5.83%)		
occurrences (all)	14		
Gastrooesophageal reflux disease			
subjects affected / exposed	14 / 223 (6.28%)		
occurrences (all)	21		
Haemorrhoids			
subjects affected / exposed	13 / 223 (5.83%)		
occurrences (all)	25		
Nausea			
subjects affected / exposed	77 / 223 (34.53%)		
occurrences (all)	133		
Stomatitis			
subjects affected / exposed	39 / 223 (17.49%)		
occurrences (all)	80		
Vomiting			
subjects affected / exposed	61 / 223 (27.35%)		
occurrences (all)	142		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	17 / 223 (7.62%)		
occurrences (all)	26		
Dry skin			
subjects affected / exposed	21 / 223 (9.42%)		
occurrences (all)	31		

Erythema			
subjects affected / exposed	19 / 223 (8.52%)		
occurrences (all)	20		
Hair colour changes			
subjects affected / exposed	55 / 223 (24.66%)		
occurrences (all)	60		
Hyperkeratosis			
subjects affected / exposed	13 / 223 (5.83%)		
occurrences (all)	21		
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	83 / 223 (37.22%)		
occurrences (all)	286		
Rash			
subjects affected / exposed	30 / 223 (13.45%)		
occurrences (all)	49		
Skin discolouration			
subjects affected / exposed	26 / 223 (11.66%)		
occurrences (all)	29		
Yellow skin			
subjects affected / exposed	22 / 223 (9.87%)		
occurrences (all)	25		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	24 / 223 (10.76%)		
occurrences (all)	34		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	31 / 223 (13.90%)		
occurrences (all)	45		
Back pain			
subjects affected / exposed	47 / 223 (21.08%)		
occurrences (all)	53		
Bone pain			
subjects affected / exposed	12 / 223 (5.38%)		
occurrences (all)	16		
Myalgia			

subjects affected / exposed	24 / 223 (10.76%)		
occurrences (all)	35		
Pain in extremity			
subjects affected / exposed	36 / 223 (16.14%)		
occurrences (all)	50		
Muscle spasms			
subjects affected / exposed	18 / 223 (8.07%)		
occurrences (all)	25		
Infections and infestations			
Gingivitis			
subjects affected / exposed	12 / 223 (5.38%)		
occurrences (all)	25		
Nasopharyngitis			
subjects affected / exposed	18 / 223 (8.07%)		
occurrences (all)	29		
Upper respiratory tract infection			
subjects affected / exposed	17 / 223 (7.62%)		
occurrences (all)	21		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	76 / 223 (34.08%)		
occurrences (all)	122		
Hyperglycaemia			
subjects affected / exposed	13 / 223 (5.83%)		
occurrences (all)	40		
Hypoalbuminaemia			
subjects affected / exposed	12 / 223 (5.38%)		
occurrences (all)	19		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 April 2007	Protocol Amendment 1 contained revisions due to UK regulations, specifically contraception needed to be defined as double barrier contraception. Secondly, serum and urine pregnancy tests prior to enrollment were specified.
13 August 2008	Protocol Amendment 2 contained revisions to: schedule of activities, study procedures and assessments (ie, urinalysis, MUGA or ECHO, ECG); introduction to include additional information; clarification of study objectives (adding an additional endpoint with regards to follow-up efficacy endpoints in previous sunitinib studies contributing to study A6181114), endpoints and study design (clarification of treatment doses for sunitinib-treated and sunitinib-naïve subjects); inclusion and exclusion criteria to reflect updated safety information in the Investigator's Brochure; clarification of study treatments; update information on AE reporting, clarify data analysis, updated ethics, definition of end of study, publication of study results, appendices (ie, Appendix 1 to include magnesium and urinalysis and updates to thyroid function testing guidance; Appendix 2 to include Response Evaluation Criteria In Solid Tumors (RECIST) and to delete Eastern Cooperative Oncology Group Performance Status [ECOG PS]; Appendix 3 to include most recent NCI CTCAE). In addition administrative changes were made.
17 May 2011	Protocol Amendment 3 contained modifications in order to allow for the inclusion of participants from a number of closing parent and extension studies and the update of protocol required text: Added/changed indications for additional parent/extension studies rolling-over participants. Included the EMA approval text for the pancreatic neuroendocrine tumor indication. In regards to study design and inclusion criteria, added the following new protocols contributing participants: A6181030, A6181064, A6181078, A6181094, A6181113, A6181120 and A6181170. Inclusion of the OS endpoint and logistics for collection of survival data for participants originating from study A6181111. Inclusion of text indicating participants on other regimens have the option (per clinical judgment) of following their parent protocol, extension protocol, or A6181114 schedule of activities and guidance on dose, dose escalation, and de-escalations. Inclusion of text to address study treatment coverage for participants on combination therapies. Inclusion of 12.5 mg dose for roll-over participants taking this dose. Inclusion of supplemental text for cases of drug-induced liver injury. Inclusion of text regarding the analyses of clinical benefit for roll-over participants who were previously on sunitinib in a parent or extension study.
21 June 2012	Protocol Amendment 4 contained revisions to: clarify language, indications, contributing protocol study numbers, ensure consistency, participant withdrawal, storage conditions, pregnancy tests, requirement for follow-up of AEs, serious AE (SAE) criteria, AEs, laboratory abnormalities, subject's legal representative, additional laboratory analyses in presence of Hy's Law cases.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported