Clinical trial results:
Prospective randomized phase-II trial with Temsirolimus versus Sunitinib in previously untreated patients with advanced or metastatic non-clear cell renal carcinoma

Summary

EudraCT number	2009-010143-13
Trial protocol	DE
Global end of trial date	02 July 2016

Results information

Result version number	v1 (current)
This version publication date	05 September 2020
First version publication date	05 September 2020

Trial information

Trial identification

Sponsor protocol code	C-II-006

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	CESAR Central European Society for Anticancer Drug Research-EWIV
Sponsor organisation address	Hangluessgasse 4/1-3, Vienna, Austria, 1150
Public contact	Prof. Viktor Grünwald, Medizinische Hochschule Hannover, 0049 5115323140, gruenwald.viktor@mh-hannover.de
Scientific contact	Dr. Max Roessler, CESAR Central European Society for Anticancer Drug Research-EWIV, 0043 1522 30 9316, max.roessler@cesar.or.at

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	30 November 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 July 2016
Global end of trial reached?	Yes
Global end of trial date	02 July 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Primary objective of the study is to demonstrate a statistical significant difference between the two arms in progression free survival (PFS) measured from randomisation until progression or death, whichever occurs first.

Protection of trial subjects:

All drugs used in the study were used according to the technical information. Procedures that determine efficacy (CT scans, MRI) and safety (blood count, blood chemistry and coagulation) are performed as in routine operations and therefore do not represent an additional burden for those patients participating in this clinical trial. Blood samples taken outside the routine for the accompanying programs do not pose any additional risk to patients. In summary, it is not possible to predict whether there will be a direct benefit for the individual patients. However, the risk for patients in the study is not higher than for patients not treated in the study. Furthermore, there is a benefit for future patients due to the progress of knowledge. It can be concluded that the benefit of this research project outweighs the risks involved.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 July 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	Germany: 22
Worldwide total number of subjects	22
EEA total number of subjects	22

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)	14
From 65 to 84 years	7
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

17 study sites in Germany were activated for patient recruitment. Only 10 of the study sites actively recruited patients into the study. Patient recruitment took place from 09Jul2009 (FPI) to 27Aug2015 (LPLV).

Pre-assignment

Screening details:

The screening criteria were defined by the inclusion and exclusion criteria as defined in the study protocol.

Period 1

Period 1 title	Treatment Phase (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

Temsirolimus is supplies in vials containing 30 mg of temsirolimus-concentrate (1.2 ml) together with a diluent (2.2 ml). When diluted, the solution contains 10 mg/ml. Temsirolimus is administered on days 1, 8, 15, 22, 29, 36 of each treatment cycle (cycle duration is 6 weeks). The recommended dose of temsirolimus for advanced renal cell carcinoma administered intravenously is 25 mg infused over a 30- to 60-minute period once weekly. Patients must be given intravenous diphenhydramine 25 to 50 mg (or similar antihistamine) approximately 30 minutes before the start of each dose of temsirolimus. Treatment is continued until disease progression.

Arm type	Experimental
Investigational medicinal product name	Temsirolimus
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Temsirolimus is supplies in vials containing 30 mg of temsirolimus-concentrate (1.2 ml) together with a diluent (2.2 ml). When diluted, the solution contains 10 mg/ml. Temsirolimus is administered on days 1, 8, 15, 22, 29, 36 of each treatment cycle (cycle duration is 6 weeks). The recommended dose of temsirolimus for advanced renal cell carcinoma administered intravenously is 25 mg infused over a 30- to 60-minute period once weekly. Patients must be given intravenous diphenhydramine 25 to 50 mg (or similar antihistamine) approximately 30 minutes before the start of each dose of temsirolimus. Treatment is continued until disease progression.

Arm title	Arm B

Arm description:

Sunitinib is available as hard capsules in 3 different strengths: 12.5 mg, 25 mf and 50 mg. 50 mg Sunitinib was administered orally on days 1-28 of each treatment cycle, followed by 2 weeks (days 29-42) of treatment pause (duration of treatment cycles 6 weeks). Treatment was continued until disease progression.

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

Dosage and administration details:

Sunitinib is available as hard capsules in 3 different strengths: 12.5 mg, 25 mf and 50 mg. 50 mg Sunitinib was administered orally on days 1-28 of each treatment cycle, followed by 2 weeks (days 29-42) of treatment pause (duration of treatment cycles 6 weeks). Treatment was continued until disease progression.

Number of subjects in period 1	Arm A	Arm B
Started	12	10
Completed	12	10

Baseline characteristics

Reporting groups

Reporting group title	Arm A

Reporting group description:

Temsirolimus is supplies in vials containing 30 mg of temsirolimus-concentrate (1.2 ml) together with a diluent (2.2 ml). When diluted, the solution contains 10 mg/ml. Temsirolimus is administered on days 1, 8, 15, 22, 29, 36 of each treatment cycle (cycle duration is 6 weeks). The recommended dose of temsirolimus for advanced renal cell carcinoma administered intravenously is 25 mg infused over a 30- to 60-minute period once weekly. Patients must be given intravenous diphenhydramine 25 to 50 mg (or similar antihistamine) approximately 30 minutes before the start of each dose of temsirolimus. Treatment is continued until disease progression.

Reporting group title	Arm B

Reporting group description:

Sunitinib is available as hard capsules in 3 different strengths: 12.5 mg, 25 mf and 50 mg. 50 mg Sunitinib was administered orally on days 1-28 of each treatment cycle, followed by 2 weeks (days 29-42) of treatment pause (duration of treatment cycles 6 weeks). Treatment was continued until disease progression.

Reporting group values	Arm A	Arm B	Total
Number of subjects	12	10	22
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	9	5	14
From 65-84 years	2	5	7
85 years and over	1	0	1
Age continuous Units: years			
arithmetic mean	57.4	64.8	
standard deviation	± 14.8	± 11.8	-
Gender categorical Units: Subjects			
Female	4	2	6
Male	8	8	16

Subject analysis sets

Subject analysis set title	Arm A
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Patients which have been randomized in Arm A of the study.

Subject analysis set title	Arm B
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Patient which have been randomized in Arm B of the study.

Reporting group values	Arm A	Arm B	
Number of subjects	12	10	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	9	5	
From 65-84 years	2	5	
85 years and over	1	0	
Age continuous Units: years			
arithmetic mean	57.4	64.8	
standard deviation	± 14.8	± 11.8	
Gender categorical Units: Subjects			
Female	4	2	
Male	8	8	

End points

End points reporting groups

Reporting group title	Arm A

Reporting group description:

Temsirolimus is supplies in vials containing 30 mg of temsirolimus-concentrate (1.2 ml) together with a diluent (2.2 ml). When diluted, the solution contains 10 mg/ml. Temsirolimus is administered on days 1, 8, 15, 22, 29, 36 of each treatment cycle (cycle duration is 6 weeks). The recommended dose of temsirolimus for advanced renal cell carcinoma administered intravenously is 25 mg infused over a 30- to 60-minute period once weekly. Patients must be given intravenous diphenhydramine 25 to 50 mg (or similar antihistamine) approximately 30 minutes before the start of each dose of temsirolimus. Treatment is continued until disease progression.

Reporting group title	Arm B

Reporting group description:

Sunitinib is available as hard capsules in 3 different strengths: 12.5 mg, 25 mf and 50 mg. 50 mg Sunitinib was administered orally on days 1-28 of each treatment cycle, followed by 2 weeks (days 29-42) of treatment pause (duration of treatment cycles 6 weeks). Treatment was continued until disease progression.

Subject analysis set title	Arm A
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Patients which have been randomized in Arm A of the study.

Subject analysis set title	Arm B
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Patient which have been randomized in Arm B of the study.

Primary: Primary Endpoint

End point title	Primary Endpoint[1]

End point description:

End point type	Primary

End point timeframe:

Date of first diagnosis until progressiv disease

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: The study has been terminated prematurely due to poor recruitment. The statistical analysis as planned in the study protocol was not done. Instead a descriptive analysis was performed.

End point values	Arm A	Arm B	Arm A	Arm B
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	12	10	12	10
Units: Months				
median (confidence interval 95%)	9.3 (1.6 to 15.9)	13.2 (1.9 to 15.9)	9.3 (1.6 to 15.9)	13.2 (1.9 to 15.9)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All information on AEs and SAEs will be reported during the treatment phase up to 4 weeks after the end of the treatment phase. Any SAEs beyond 28 days after the last dose of study medication considered related to the study medication will be reported.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Arm A

Reporting group description:

Temsirolimus is supplies in vials containing 30 mg of temsirolimus-concentrate (1.2 ml) together with a diluent (2.2 ml). When diluted, the solution contains 10 mg/ml. Temsirolimus is administered on days 1, 8, 15, 22, 29, 36 of each treatment cycle (cycle duration is 6 weeks). The recommended dose of temsirolimus for advanced renal cell carcinoma administered intravenously is 25 mg infused over a 30- to 60-minute period once weekly. Patients must be given intravenous diphenhydramine 25 to 50 mg (or similar antihistamine) approximately 30 minutes before the start of each dose of temsirolimus. Treatment is continued until disease progression.

Reporting group title	Arm B

Reporting group description:

Sunitinib is available as hard capsules in 3 different strengths: 12.5 mg, 25 mf and 50 mg. 50 mg Sunitinib was administered orally on days 1-28 of each treatment cycle, followed by 2 weeks (days 29-42) of treatment pause (duration of treatment cycles 6 weeks). Treatment was continued until disease progression.

Serious adverse events	Arm A	Arm B	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 12 (58.33%)	6 / 10 (60.00%)	
number of deaths (all causes)	7	5	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to peritoneum			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular disorders			
Lymphoedema			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			

Lymphadenectomy			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Fatigue			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
local swelling			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
multi-organ failure			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			

subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 12 (0.00%)	2 / 10 (20.00%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Hemiparesis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	0 / 12 (0.00%)	2 / 10 (20.00%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 12 (0.00%)	2 / 10 (20.00%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess neck			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis infective			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumonia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
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 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Arm A	Arm B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 12 (91.67%)	10 / 10 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acrochordon			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Tumour pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Haematoma			

subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Hot flush			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Hypertension			
subjects affected / exposed	2 / 12 (16.67%)	2 / 10 (20.00%)	
occurrences (all)	2	3	
Hypotension			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Lymphoedema			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Chest pain			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Chills			
subjects affected / exposed	2 / 12 (16.67%)	1 / 10 (10.00%)	
occurrences (all)	2	2	
Fatigue			
subjects affected / exposed	2 / 12 (16.67%)	5 / 10 (50.00%)	
occurrences (all)	4	12	
Feeling cold			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
local swelling			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Mucosal inflammation			

subjects affected / exposed	4 / 12 (33.33%)	4 / 10 (40.00%)	
occurrences (all)	4	5	
Oedema			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	3 / 12 (25.00%)	0 / 10 (0.00%)	
occurrences (all)	3	0	
Pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Peripheral swelling			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Pyrexia			
subjects affected / exposed	3 / 12 (25.00%)	1 / 10 (10.00%)	
occurrences (all)	25	1	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Oral herpes			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Pelvic pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
vaginal inflammation			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Dysphonia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Dyspnoea			
subjects affected / exposed	4 / 12 (33.33%)	0 / 10 (0.00%)	
occurrences (all)	4	0	
Epistaxis			
subjects affected / exposed	1 / 12 (8.33%)	2 / 10 (20.00%)	
occurrences (all)	1	2	
Haemoptysis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Oropharyngeal pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Pleural effusion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Pleurisy			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Sleep disorder			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	
occurrences (all)	3	0	
Tension			

subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	3	0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Blood cholesterol increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	6	0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
C-reactive protein increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Haemoglobin decreased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Low density lipoprotein increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	4	0	
Weight decreased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	2	
Weight increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Wound			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Nervous system disorders			

Ageusia			
subjects affected / exposed	0 / 12 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	5	
Dizziness			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Dysgeusia			
subjects affected / exposed	4 / 12 (33.33%)	3 / 10 (30.00%)	
occurrences (all)	4	3	
Headache			
subjects affected / exposed	2 / 12 (16.67%)	2 / 10 (20.00%)	
occurrences (all)	3	2	
Intercostal neuralgia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Neuropathy peripheral			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Paraesthesia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
anemia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Leukopenia			
subjects affected / exposed	0 / 12 (0.00%)	3 / 10 (30.00%)	
occurrences (all)	0	5	
neutopenia			
subjects affected / exposed	0 / 12 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	2	
Thrombocytopenia			
subjects affected / exposed	0 / 12 (0.00%)	3 / 10 (30.00%)	
occurrences (all)	0	6	
Ear and labyrinth disorders			

Inner ear inflammation			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Middle ear effusion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Vertigo			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	
occurrences (all)	2	1	
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Eye oedema			
subjects affected / exposed	1 / 12 (8.33%)	2 / 10 (20.00%)	
occurrences (all)	1	2	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Abdominal pain			
subjects affected / exposed	5 / 12 (41.67%)	1 / 10 (10.00%)	
occurrences (all)	9	2	
Abdominal pain upper			
subjects affected / exposed	3 / 12 (25.00%)	1 / 10 (10.00%)	
occurrences (all)	3	1	
Cheilitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	3 / 12 (25.00%)	1 / 10 (10.00%)	
occurrences (all)	4	1	
Diarrhoea			
subjects affected / exposed	3 / 12 (25.00%)	2 / 10 (20.00%)	
occurrences (all)	3	4	
Dry mouth			

subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)		
occurrences (all)	1	1		
Dyspepsia				
subjects affected / exposed	1 / 12 (8.33%)	5 / 10 (50.00%)		
occurrences (all)	1	10		
Dysphagia				
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)		
occurrences (all)	1	0		
Epigastric discomfort				
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)		
occurrences (all)	0	1		
Flatulence				
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)		
occurrences (all)	1	2		
Gastritis				
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)		
occurrences (all)	2	0		
Haemorrhoids				
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)		
occurrences (all)	0	1		
Mouth ulceration				
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)		
occurrences (all)	2	0		
Nausea				
subjects affected / exposed	3 / 12 (25.00%)	5 / 10 (50.00%)		
occurrences (all)	6	11		
Oral pain				
subjects affected / exposed	2 / 12 (16.67%)	1 / 10 (10.00%)		
occurrences (all)	2	1		
Stomatitis				
subjects affected / exposed	4 / 12 (33.33%)	3 / 10 (30.00%)		
occurrences (all)	7	3		
Tongue discolouration				
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)		
occurrences (all)	0	1		
Vomiting				

subjects affected / exposed	2 / 12 (16.67%)	3 / 10 (30.00%)	
occurrences (all)	2	4	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	3	0	
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	0 / 12 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	3	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Alopecia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Dry skin			
subjects affected / exposed	1 / 12 (8.33%)	2 / 10 (20.00%)	
occurrences (all)	1	2	
Erythema			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Hair colour changes			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Hyperhidrosis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Nail disorder			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Night sweats			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Onychoclasis			

subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	1 / 12 (8.33%)	3 / 10 (30.00%)	
occurrences (all)	1	4	
Pruritus			
subjects affected / exposed	5 / 12 (41.67%)	0 / 10 (0.00%)	
occurrences (all)	6	0	
Rash			
subjects affected / exposed	6 / 12 (50.00%)	1 / 10 (10.00%)	
occurrences (all)	9	1	
Skin erosion			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	
occurrences (all)	1	2	
Skin fissures			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Skin lesion			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Xeroderma			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Yellow skin			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	5	
Renal and urinary disorders			
Bladder irritation			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Renal failure			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	2	
Back pain			
subjects affected / exposed	2 / 12 (16.67%)	1 / 10 (10.00%)	
occurrences (all)	3	1	
Bone pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Flank pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Intervertebral disc protrusion			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
monarthritis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	3	0	
Musculoskeletal pain			
subjects affected / exposed	2 / 12 (16.67%)	1 / 10 (10.00%)	
occurrences (all)	2	1	
Musculoskeletal stiffness			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Myofascial pain syndrome			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Neck pain			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	
occurrences (all)	4	0	

Osteoarthritis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Pain in extremity			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	
occurrences (all)	3	1	
Spinal pain			
subjects affected / exposed	3 / 12 (25.00%)	0 / 10 (0.00%)	
occurrences (all)	5	0	
Infections and infestations			
Abscess oral			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Tonsillitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Anal fungal infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	2	
Bronchitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Folliculitis			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	
occurrences (all)	4	0	
Fungal infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Furuncle			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Genital herpes zoster			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Gingivitis			

subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Herpes zoster			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Laryngitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Mastoiditis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	2 / 12 (16.67%)	1 / 10 (10.00%)	
occurrences (all)	5	1	
Oesophageal candidiasis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Oral candidiasis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	2 / 12 (16.67%)	1 / 10 (10.00%)	
occurrences (all)	2	1	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			

Cachexia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Decreased appetite			
subjects affected / exposed	4 / 12 (33.33%)	3 / 10 (30.00%)	
occurrences (all)	5	8	
Hypercholesterolaemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Hyperglycaemia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Hyperlipidaemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Hypertriglyceridaemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	6	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 March 2010	In a new product information for Sunitinib fistula formation was included as a potential adverse event. This was incorporated into the study protocol and informed consent.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported