



Clinical trial results:

A Phase I Study of Sunitinib (SU11248), an Oral Multi-Targeted Tyrosine Kinase Inhibitor, in Children with Refractory Solid Tumors

Summary

EudraCT number	2012-000690-23
Trial protocol	Outside EU/EEA
Global end of trial date	12 July 2012

Results information

Result version number	v1 (current)
This version publication date	14 April 2018
First version publication date	14 April 2018

Trial information

Trial identification

Sponsor protocol code	ADVL0612;NCI-07-C-0220
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00387920
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 110017
Public contact	Biljana Georgievska, Childrens Oncology Group – Phase 1/Pilot Consortium, 001 6262411566, bgeorgievska@childrensoncologyrgroup.org
Scientific contact	Biljana Georgievska, Childrens Oncology Group – Phase 1/Pilot Consortium, 001 6262411566, bgeorgievska@childrensoncologyrgroup.org

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-000342-PIP01-08
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes
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	18 June 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 July 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To determine the maximum tolerated dose (MTD) and recommend a Phase 2 dose of sunitinib administered orally once daily for 28 days followed by 14 days rest period in children with refractory solid tumours.
- To define and describe the toxicities of sunitinib administered on this schedule.
- To characterize the pharmacokinetics of oral sunitinib in children with refractory solid tumours.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 2007
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	26 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 35
Worldwide total number of subjects	35
EEA total number of subjects	0

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)	16

Adolescents (12-17 years)	16
Adults (18-64 years)	3
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 35 subjects were enrolled and treated in the study from 01-Dec-2007 to 12-Jul-2012.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A: Sunitinib 15 mg/m ²

Arm description:

Subjects with recurrent or refractory solid tumour received 15 milligram per meter square (mg/m²) of sunitinib orally, once daily for 28 days in each cycle of 42 days.

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

Dosage and administration details:

Subjects were administered 15 mg/m² capsule of sunitinib based on the body surface area (BSA) once daily.

Arm title	Part A: Sunitinib 20 mg/m ²
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Arm description:

Subjects with recurrent or refractory solid tumour received 20 mg/m² of sunitinib orally, once daily for 28 days in each cycle of 42 days.

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

Dosage and administration details:

Subjects were administered 20 mg/m² capsule of sunitinib based on the BSA once daily.

Arm title	Part B: Sunitinib 15 mg/m ²
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Arm description:

Subjects with recurrent or refractory solid tumour received 15 mg/m² of sunitinib orally, once daily for 28 days in each cycle of 42 days.

Arm type	Experimental
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Investigational medicinal product name	Sunitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Subjects were administered 15 mg/m ² capsule of sunitinib based on the BSA once daily.	
Arm title	Part B: Sunitinib 20 mg/m ²

Arm description:

Subjects with recurrent or refractory solid tumour received 20 mg/m² of sunitinib orally, once daily for 28 days in each cycle of 42 days.

Arm type	Experimental
Investigational medicinal product name	Sunitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Subjects were administered 20 mg/m ² capsule of sunitinib based on the BSA once daily.	
Arm title	Part C: Sunitinib 15 mg/m ²

Arm description:

Subjects with recurrent or refractory solid tumour received 15 mg/m² of sunitinib orally, once daily for 28 days in each cycle of 42 days.

Arm type	Experimental
Investigational medicinal product name	Sunitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral solution
Routes of administration	Oral use
Dosage and administration details:	
Subjects were administered 15 mg/m ² sunitinib as a powder sprinkled on applesauce or yogurt as per BSA once daily.	

Number of subjects in period 1	Part A: Sunitinib 15 mg/m ²	Part A: Sunitinib 20 mg/m ²	Part B: Sunitinib 15 mg/m ²
Started	6	6	8
Completed	0	0	2
Not completed	6	6	6
Consent withdrawn by subject	-	-	1
Adverse event	2	3	1
Insufficient clinical response	4	3	4

Number of subjects in period 1	Part B: Sunitinib 20 mg/m ²	Part C: Sunitinib 15 mg/m ²
Started	3	12
Completed	0	1
Not completed	3	11
Consent withdrawn by subject	1	2

Adverse event	-	1
Insufficient clinical response	2	8

Baseline characteristics

Reporting groups

Reporting group title	Part A: Sunitinib 15 mg/m ²
Reporting group description: Subjects with recurrent or refractory solid tumour received 15 milligram per meter square (mg/m ²) of sunitinib orally, once daily for 28 days in each cycle of 42 days.	
Reporting group title	Part A: Sunitinib 20 mg/m ²
Reporting group description: Subjects with recurrent or refractory solid tumour received 20 mg/m ² of sunitinib orally, once daily for 28 days in each cycle of 42 days.	
Reporting group title	Part B: Sunitinib 15 mg/m ²
Reporting group description: Subjects with recurrent or refractory solid tumour received 15 mg/m ² of sunitinib orally, once daily for 28 days in each cycle of 42 days.	
Reporting group title	Part B: Sunitinib 20 mg/m ²
Reporting group description: Subjects with recurrent or refractory solid tumour received 20 mg/m ² of sunitinib orally, once daily for 28 days in each cycle of 42 days.	
Reporting group title	Part C: Sunitinib 15 mg/m ²
Reporting group description: Subjects with recurrent or refractory solid tumour received 15 mg/m ² of sunitinib orally, once daily for 28 days in each cycle of 42 days.	

Reporting group values	Part A: Sunitinib 15 mg/m ²	Part A: Sunitinib 20 mg/m ²	Part B: Sunitinib 15 mg/m ²
Number of subjects	6	6	8
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	16.3	12.8	10.5
standard deviation	± 3.3	± 1.9	± 5.3
Gender categorical Units: Subjects			
Female	2	2	5
Male	4	4	3

Reporting group values	Part B: Sunitinib 20 mg/m ²	Part C: Sunitinib 15 mg/m ²	Total
Number of subjects	3	12	35
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	9.7	12.1	
standard deviation	± 3.5	± 5.2	-

Gender categorical			
Units: Subjects			
Female	3	7	19
Male	0	5	16

End points

End points reporting groups

Reporting group title	Part A: Sunitinib 15 mg/m ²
Reporting group description: Subjects with recurrent or refractory solid tumour received 15 milligram per meter square (mg/m ²) of sunitinib orally, once daily for 28 days in each cycle of 42 days.	
Reporting group title	Part A: Sunitinib 20 mg/m ²
Reporting group description: Subjects with recurrent or refractory solid tumour received 20 mg/m ² of sunitinib orally, once daily for 28 days in each cycle of 42 days.	
Reporting group title	Part B: Sunitinib 15 mg/m ²
Reporting group description: Subjects with recurrent or refractory solid tumour received 15 mg/m ² of sunitinib orally, once daily for 28 days in each cycle of 42 days.	
Reporting group title	Part B: Sunitinib 20 mg/m ²
Reporting group description: Subjects with recurrent or refractory solid tumour received 20 mg/m ² of sunitinib orally, once daily for 28 days in each cycle of 42 days.	
Reporting group title	Part C: Sunitinib 15 mg/m ²
Reporting group description: Subjects with recurrent or refractory solid tumour received 15 mg/m ² of sunitinib orally, once daily for 28 days in each cycle of 42 days.	
Subject analysis set title	Part B: Sunitinib (All subjects)
Subject analysis set type	Full analysis
Subject analysis set description: Subjects with recurrent or refractory solid tumour received either 15 or 20 mg/m ² of sunitinib orally, once daily for 28 days in each cycle of 42 days.	

Primary: Maximum Tolerated Dose (MTD)

End point title	Maximum Tolerated Dose (MTD) ^[1]
End point description: The MTD was defined as the highest dose at which no more than 1 of 6 participants or no more than 1 of 3 participants experienced a dose Limiting Toxicity (DLT). DLT defined as any of the following occurring during cycle 1 of part 1 of study, Hematologic toxicity: Any grade 4 or higher hematologic adverse event, Grade 4 thrombocytopenia or neutropenia. Nonhematologic toxicity: grade 3 non-hematologic toxicity except grade 3 or higher laboratory AE which was asymptomatic and rapidly reversible adverse events (returned to baseline or to grade 1 or lower within 7 days), Grade 3 nausea and vomiting of less than (<)3 days, Grade 3 fever of <5 days, Grade 3 aspartate transaminase, alanine transaminase and bilirubin (returned to grade 2 or lower within 7 days). Grades based on NCICTC for Adverse Events version 4.03. Per-protocol set included all enrolled subjects who received at least one dose of study drug.	
End point type	Primary
End point timeframe: Cycle 1 (Day 1 up to Day 42)	

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: Part B 20 mg/m² was evaluated and exceed MTD due to 2 out of 3 patients with DLT, then MTD was established at the lower level as 15 mg /m².

End point values	Part B: Sunitinib (All subjects)			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: mg per meter square				
number (not applicable)	15			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Subjects With Treatment Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs)
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End point description:

An AE was any untoward medical occurrence in a subject who received investigational product without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly; lack of efficacy in an approved indication. Treatment-emergent are events between first dose of study drug and up to 30 days after last dose of study drug that were absent before treatment or that worsened relative to pretreatment state. Per-protocol set included all enrolled subjects who received at least one dose of study drug.

End point type	Secondary
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End point timeframe:

Baseline up to 30 days after last dose of study drug (maximum duration: Part A: 4 cycles, Part B: 9 cycles, Part C: 18 cycles)

End point values	Part A: Sunitinib 15 mg/m ²	Part A: Sunitinib 20 mg/m ²	Part B: Sunitinib 15 mg/m ²	Part B: Sunitinib 20 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	8	3
Units: Subjects				
AEs	6	6	8	3
SAEs	3	3	3	3

End point values	Part C: Sunitinib 15 mg/m ²			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Subjects				
AEs	12			
SAEs	6			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment Related Adverse Events

End point title	Number of Subjects With Treatment Related Adverse Events
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End point description:

Treatment-related AE was any untoward medical occurrence attributed to study drug in a subject who received study drug. Relatedness to study drug was assessed by the investigator. Per protocol set included all enrolled subjects who received at least one dose of study drug.

End point type	Secondary
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End point timeframe:

Baseline up to 30 days after last dose of study drug (maximum duration: Part A: 4 cycles, Part B: 9 cycles, Part C: 18 cycles)

End point values	Part A: Sunitinib 15 mg/m ²	Part A: Sunitinib 20 mg/m ²	Part B: Sunitinib 15 mg/m ²	Part B: Sunitinib 20 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	8	3
Units: Subjects	6	6	8	3

End point values	Part C: Sunitinib 15 mg/m ²			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Subjects	12			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Adverse Events (AEs) According to Maximum Severity

End point title	Number of Subjects With Adverse Events (AEs) According to Maximum Severity
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End point description:

An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. AE was assessed according to maximum severity grading based on

National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0. Grade 1 =mild; Grade 2 =moderate; within normal limits, Grade 3 =severe or medically significant but not immediately life-threatening; Grade 4 =life-threatening or disabling; urgent intervention indicated; Grade 5 =death. Per protocol set included all enrolled subjects who received at least one dose of study drug.

End point type	Secondary
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End point timeframe:

Baseline up to 30 days after last dose of study drug (maximum duration: Part A: 4 cycles, Part B: 9 cycles, Part C: 18 cycles)

End point values	Part A: Sunitinib 15 mg/m ²	Part A: Sunitinib 20 mg/m ²	Part B: Sunitinib 15 mg/m ²	Part B: Sunitinib 20 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	8	3
Units: Subjects				
Grade 1	0	0	2	0
Grade 2	1	1	2	0
Grade 3	4	4	3	1
Grade 4	1	1	1	1
Grade 5	0	0	0	1

End point values	Part C: Sunitinib 15 mg/m ²			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Subjects				
Grade 1	0			
Grade 2	1			
Grade 3	7			
Grade 4	0			
Grade 5	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Laboratory Abnormalities By Severity: National Cancer Institute Common Terminology Criteria for Adverse Event (Version 4.0) Grade 1 to 4 Hematological and Chemistry Test Abnormalities

End point title	Number of subjects with Laboratory Abnormalities By Severity: National Cancer Institute Common Terminology Criteria for Adverse Event (Version 4.0) Grade 1 to 4 Hematological and Chemistry Test Abnormalities
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End point description:

Anemia(grade[g]1:Less than[<] Lower limit of normal[LLN] to 10gram per[/] deciliter[g/dL],g2:<10 to 8g/dL,g3:<8g/dL,g4:lifethreatening);platelet (g1:<LLN to 75*10³/millimeter[mm]³,g2:

<75*10³/mm³ to 50*10³/mm³,g3:<50*10³/mm³ to 25*10³/mm³,g4:<25*10³/mm³); white blood cell count (WBC)(g1:<LLN to 3*10³/mm³,g2:<3*10³ to 2*10³/mm³,g3:<2*10³ to 1*10³/mm³,g4:<1*10³/mm³); ALT/AST(grade[g]1:>ULN-3*ULN,g2:>3-5*ULN,g3:>5-20*ULN,g4:>20*ULN);CR(g1:>ULN-1.5*ULN,g2:>1.5-3*ULN,g3:>3-6*ULN,g4:>6*ULN););bilirubin(total)(g1:>ULN-1.5*ULN,g2:>1.5-3*ULN,g3:>3-10*ULN,g4:>10*ULN); hypophosphatemia(g1:<LLN-2.5mg/dL,g2:<2.5-2mg/dL,g3:<2-1mg/dL,g4:<1mg/dL);hypocalcemia(g1:<LLN-8mg/dL,g2:<8-7mg/dL,g3:<7-6mg/dL,g4:<6mg/dL);amylase,lipase(g1:>ULN-1.5*ULN,g2:>1.5-2.0*ULN,g3:>2.0-5.0*ULN;>5.0*ULN); hypercalcemia(g1:>ULN-11.5mg/dL,g2:>11.5-12.5mg/dL,g3:>12.5-13.5mg/dL,g4:>13.5mg/dL).Only categories with atleast 1 subject with abnormality are reported in this

End point type	Secondary
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End point timeframe:

Baseline up to 30 days after last dose of study drug (maximum duration: Part A: 4 cycles, Part B: 9 cycles, Part C: 18 cycles)

End point values	Part A: Sunitinib 15 mg/m ²	Part A: Sunitinib 20 mg/m ²	Part B: Sunitinib 15 mg/m ²	Part B: Sunitinib 20 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	8	3
Units: Subjects				
Anemia: Grade 2 (n =6,6,8,3,12)	0	2	0	0
Anemia: Grade 3 (n =6,6,8,3,12)	0	0	0	0
Platelets: Grade 2 (n =6,6,8,3,12)	0	2	0	0
WBC: Grade 2 (n =6,6,8,3,12)	1	1	0	0
WBC: Grade 3 (n =6,6,8,3,12)	0	3	0	0
Amylase: Grade 1 (n =6,6,8,3,12)	0	2	1	0
AST: Grade 1 (n =4,6,0,0,2)	2	5	99999	99999
Creatinine: Grade 1 (n =6,6,8,3,12)	5	6	6	3
Creatinine: Grade 2 (n =6,6,8,3,12)	0	0	2	0
Hypophosphatemia: Grade 1 (n =6,6,8,3,12)	1	4	1	0
Hypophosphatemia: Grade 2 (n =6,6,8,3,12)	0	1	0	0
Hypophosphatemia: Grade 3 (n =6,6,8,3,12)	1	0	1	0
Hypophosphatemia: Grade 4 (n =6,6,8,3,12)	0	0	0	0
Lipase: Grade 1 (n =6,6,8,3,12)	0	0	2	1
Lipase: Grade 2 (n =6,6,8,3,12)	0	1	0	0
Lipase: Grade 3 (n =6,6,8,3,12)	0	1	0	0
Hypercalcemia: Grade 1 (n =0,0,0,0,12)	99999	99999	99999	99999
Hypocalcemia: Grade 1 (n =0,0,0,0,4)	99999	99999	99999	99999

End point values	Part C: Sunitinib 15 mg/m ²			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Subjects				
Anemia: Grade 2 (n =6,6,8,3,12)	0			
Anemia: Grade 3 (n =6,6,8,3,12)	1			

Platelets: Grade 2 (n =6,6,8,3,12)	1			
WBC: Grade 2 (n =6,6,8,3,12)	3			
WBC: Grade 3 (n =6,6,8,3,12)	0			
Amylase: Grade 1 (n =6,6,8,3,12)	1			
AST: Grade 1 (n =4,6,0,0,2)	1			
Creatinine: Grade 1 (n =6,6,8,3,12)	10			
Creatinine: Grade 2 (n =6,6,8,3,12)	0			
Hypophosphatemia: Grade 1 (n =6,6,8,3,12)	1			
Hypophosphatemia: Grade 2 (n =6,6,8,3,12)	0			
Hypophosphatemia: Grade 3 (n =6,6,8,3,12)	0			
Hypophosphatemia: Grade 4 (n =6,6,8,3,12)	0			
Lipase: Grade 1 (n =6,6,8,3,12)	1			
Lipase: Grade 2 (n =6,6,8,3,12)	1			
Lipase: Grade 3 (n =6,6,8,3,12)	0			
Hypercalcemia: Grade 1 (n =0,0,0,0,12)	3			
Hypocalcemia: Grade 1 (n =0,0,0,0,4)	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of Sunitinib and its metabolite

End point title	Maximum Observed Plasma Concentration (Cmax) of Sunitinib and its metabolite ^[2]
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End point description:

SU012662 was the metabolite of sunitinib. Pharmacokinetic (PK) population included all treated subjects who received at least one dose of study drug. Data for part B: 20 mg/m² arm was not evaluable as the plasma concentration for this arm at the pre-specified time points was 0. Here, 99999 signifies data was not evaluable as only 1 subject was analyzed.

End point type	Secondary
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End point timeframe:

Pre-dose (0 hour), 1, 2, 4, 6, 8, 10, 24, 25, 26, 27, 28, 48, 49, 50, 51, 52 hours post-dose on Day 1 of Cycle 1

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data for part B: 20 mg/m² arm was not evaluable as the plasma concentration for this arm at the pre-specified time points was 0.

End point values	Part A: Sunitinib 15 mg/m ²	Part A: Sunitinib 20 mg/m ²	Part B: Sunitinib 15 mg/m ²	Part C: Sunitinib 15 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	1	4	12
Units: Nanogram per milliliter				
geometric mean (geometric coefficient of variation)				
Sunitinib	15.2074 (± 16)	99999 (± 99999)	22.5757 (± 91)	18.9275 (± 52)

SU012662	2.42764 (\pm 54)	99999 (\pm 99999)	3.45750 (\pm 102)	1.755 (\pm 13249)
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Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Observed Plasma Concentration (Tmax) of Sunitinib and its metabolite

End point title	Time to Reach Maximum Observed Plasma Concentration (Tmax) of Sunitinib and its metabolite ^[3]
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End point description:

SU012662 was the metabolite of sunitinib. PK population included all treated subjects who received at least one dose of study drug. Data for part B: 20 mg/m² arm was not evaluable as the plasma concentration for this arm at the pre-specified time points was 0.

End point type	Secondary
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End point timeframe:

Pre-dose (0 hour), 1, 2, 4, 6, 8, 10, 24, 25, 26, 27, 28, 48, 49, 50, 51, 52 hours post-dose on Day 1 of Cycle 1

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Data for part B: 20 mg/m² arm was not evaluable as the plasma concentration for this arm at the pre-specified time points was 0.

End point values	Part A: Sunitinib 15 mg/m ²	Part A: Sunitinib 20 mg/m ²	Part B: Sunitinib 15 mg/m ²	Part C: Sunitinib 15 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	1	4	12
Units: Hour				
median (full range (min-max))				
Sunitinib	7.00 (4.00 to 48.0)	8.00 (8.00 to 8.00)	7.00 (2.00 to 8.00)	4.00 (4.00 to 8.00)
SU012662	28.0 (6.00 to 48.0)	8.00 (8.00 to 8.00)	7.00 (4.00 to 8.00)	6.00 (4.00 to 24.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to the last quantifiable Time Point (Tlast) of Sunitinib and its metabolite

End point title	Time to the last quantifiable Time Point (Tlast) of Sunitinib and its metabolite ^[4]
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End point description:

SU012662 was the metabolite of sunitinib. PK population included all treated subjects who received at least one dose of study drug. Data for part B: 20 mg/m² arm was not evaluable as the plasma concentration for this arm at the pre-specified time points was 0.

End point type	Secondary
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End point timeframe:

Pre-dose (0 hour), 1, 2, 4, 6, 8, 10, 24, 25, 26, 27, 28, 48, 49, 50, 51, 52 hours post-dose on Day 1 of Cycle 1

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data for part B: 20 mg/m² arm was not evaluable as the plasma concentration for this arm at the pre-specified time points was 0.

End point values	Part A: Sunitinib 15 mg/m ²	Part A: Sunitinib 20 mg/m ²	Part B: Sunitinib 15 mg/m ²	Part C: Sunitinib 15 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	1	4	12
Units: Hour				
median (full range (min-max))				
Sunitinib	48.0 (48.0 to 48.0)	48.0 (48.0 to 48.0)	48.0 (48.0 to 48.0)	48.0 (48.0 to 48.0)
SU012662	48.0 (48.0 to 48.0)	48.0 (48.0 to 48.0)	48.0 (24.0 to 48.0)	48.0 (48.0 to 48.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under The Plasma Concentration-Time Curve From Time Zero to Last Quantifiable Concentration of Sunitinib and its metabolite

End point title	Area Under The Plasma Concentration-Time Curve From Time Zero to Last Quantifiable Concentration of Sunitinib and its metabolite ^[5]
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End point description:

AUC (last) is the area under the plasma concentration versus time curve from time zero (pre-dose) to last quantifiable concentration. SU012662 was the metabolite of sunitinib. PK population included all treated subjects who received at least one dose of study drug. Data for part B: 20 mg/m² arm was not evaluable as the plasma concentration for this arm at the pre-specified time points was 0. Here, 99999 signifies data was not evaluable as only 1 subject was analyzed.

End point type	Secondary
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End point timeframe:

Pre-dose (0 hour), 1, 2, 4, 6, 8, 10, 24, 25, 26, 27, 28, 48, 49, 50, 51, 52 hours post-dose on Day 1 of Cycle 1

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data for part B: 20 mg/m² arm was not evaluable as the plasma concentration for this arm at the pre-specified time points was 0.

End point values	Part A: Sunitinib 15 mg/m ²	Part A: Sunitinib 20 mg/m ²	Part B: Sunitinib 15 mg/m ²	Part C: Sunitinib 15 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	1	4	12
Units: Nanogram*hour per milliliter (ng*hr/mL)				
geometric mean (geometric coefficient of variation)				

Sunitinib	457.425 (± 8)	99999 (± 99999)	546.296 (± 70)	481.659 (± 50)
SU012662	80.5142 (± 38)	99999 (± 99999)	106.070 (± 119)	46.7130 (± 519121)

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under The Plasma Concentration-Time Curve From Time 0 to 24 Hours (AUC [0-24]) of Sunitinib and its metabolite

End point title	Area Under The Plasma Concentration-Time Curve From Time 0 to 24 Hours (AUC [0-24]) of Sunitinib and its metabolite ^[6]
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End point description:

AUC (0-24) is the area under the plasma concentration versus time curve from time zero (pre-dose) to 12 hours post-dose. SU012662 was the metabolite of sunitinib. PK population included all treated subjects who received at least one dose of study drug. Data for part B: 20 mg/m² arm was not evaluable as the plasma concentration for this arm at the pre-specified time points was 0. Here, 99999 signifies data was not evaluable as only 1 subject was analyzed.

End point type	Secondary
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End point timeframe:

Pre-dose (0 hour), 1, 2, 4, 6, 8, 10, 24 hours post-dose on Day 1 of Cycle 1

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data for part B: 20 mg/m² arm was not evaluable as the plasma concentration for this arm at the pre-specified time points was 0.

End point values	Part A: Sunitinib 15 mg/m ²	Part A: Sunitinib 20 mg/m ²	Part B: Sunitinib 15 mg/m ²	Part C: Sunitinib 15 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	1	4	12
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)				
Sunitinib	241.643 (± 15)	99999 (± 99999)	351.002 (± 73)	312.669 (± 50)
SU012662	33.8460 (± 25)	99999 (± 99999)	63.9279 (± 91)	25.7630 (± 253329)

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under The Plasma Concentration-Time Curve From Time 0 to 48 Hours (AUC [0-48]) of Sunitinib and its metabolite

End point title	Area Under The Plasma Concentration-Time Curve From Time 0 to 48 Hours (AUC [0-48]) of Sunitinib and its metabolite ^[7]
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End point description:

AUC (0-48) is the area under the plasma concentration versus time curve from time zero (pre-dose) to 48 hours post-dose. SU012662 was the metabolite of sunitinib. PK population included all treated

subjects who received at least one dose of study drug. Data for part B: 20 mg/m² arm was not evaluable as the plasma concentration for this arm at the pre-specified time points was 0.

End point type	Secondary
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End point timeframe:

Pre-dose (0 hour), 1, 2, 4, 6, 8, 10, 24, 25, 26, 27, 28, 48 hours post-dose on Day 1 of Cycle 1

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data for part B: 20 mg/m² arm was not evaluable as the plasma concentration for this arm at the pre-specified time points was 0.

End point values	Part A: Sunitinib 15 mg/m ²	Part A: Sunitinib 20 mg/m ²	Part B: Sunitinib 15 mg/m ²	Part C: Sunitinib 15 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	1	4	12
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)				
Sunitinib	457.425 (± 8)	99999 (± 99999)	546.296 (± 70)	481.659 (± 50)
SU012662	80.5142 (± 38)	99999 (± 99999)	118.128 (± 93)	46.7130 (± 519121)

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under The Plasma Concentration-Time Curve From Time Zero to Infinity of Sunitinib and its metabolite

End point title	Area Under The Plasma Concentration-Time Curve From Time Zero to Infinity of Sunitinib and its metabolite ^[8]
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End point description:

AUC (inf) is the area under the plasma concentration versus time curve from time zero (pre-dose) extrapolated to infinity. SU012662 was the metabolite of Sunitinib. PK population included all treated subjects who received at least one dose of study drug. Data for part B: 20 mg/m² arm was not evaluable as the plasma concentration for this arm at the pre-specified time points was 0. Here, number of subjects analyzed (N) signifies number of subjects evaluable for this endpoint and n signifies number of subjects evaluable at specified time points only. Here, 99999 signifies data was not evaluable as only 1 subject was analyzed.

End point type	Secondary
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End point timeframe:

Pre-dose (0 hour), 1, 2, 4, 6, 8, 10, 24, 25, 26, 27, 28, 48, 49, 50, 51, 52 hours post-dose on Day 1 of Cycle 1

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data for part B: 20 mg/m² arm was not evaluable as the plasma concentration for this arm at the pre-specified time points was 0.

End point values	Part A: Sunitinib 15 mg/m ²	Part A: Sunitinib 20 mg/m ²	Part B: Sunitinib 15 mg/m ²	Part C: Sunitinib 15 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	1	4	12
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)				
Sunitinib (n =3, 1, 4, 12)	1410.56 (± 167)	99999 (± 99999)	848.275 (± 101)	658.225 (± 54)
SU012662 (n =1, 1, 3, 8)	99999 (± 99999)	99999 (± 99999)	1078.81 (± 133)	402.415 (± 74)

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Elimination Half-Life (t_{1/2}) of Sunitinib and its metabolite

End point title	Terminal Elimination Half-Life (t _{1/2}) of Sunitinib and its metabolite ^[9]
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End point description:

Terminal elimination (plasma decay) half-life is the time measured for the plasma concentration to decrease by one half. SU012662 was the metabolite of sunitinib. PK population included all treated subjects who received at least one dose of study drug. Data for part B: 20 mg/m² arm was not evaluable as the plasma concentration for this arm at the pre-specified time points was 0. Here, N signifies number of subjects evaluable for this endpoint and n signifies number of subjects evaluable at specified time points only. Here, 99999 signifies data was not evaluable as only 1 subject was analyzed.

End point type	Secondary
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End point timeframe:

Pre-dose (0 hour), 1, 2, 4, 6, 8, 10, 24, 25, 26, 27, 28, 48, 49, 50, 51, 52 hours post-dose on Day 1 of Cycle 1

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data for part B: 20 mg/m² arm was not evaluable as the plasma concentration for this arm at the pre-specified time points was 0.

End point values	Part A: Sunitinib 15 mg/m ²	Part A: Sunitinib 20 mg/m ²	Part B: Sunitinib 15 mg/m ²	Part C: Sunitinib 15 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	1	4	12
Units: Hour				
arithmetic mean (standard deviation)				
Sunitinib (n =3, 1, 4, 12)	115.2 (± 143.65)	99999 (± 99999)	33.08 (± 28.975)	24.05 (± 8.2705)
SU012662 (n =1, 1, 3, 8)	99999 (± 99999)	99999 (± 99999)	502.6 (± 726.21)	85.79 (± 108.94)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Objective Response

End point title	Percentage of Subjects With Objective Response
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End point description:

Percentage of subjects with confirmed complete response (CR) and partial response (PR) were based on RECIST v1.1. CR: Disappearance of all non-nodal target and non-target lesions, including target and non-target lymph nodes reduction to <10 millimeter (mm) in short axis. No new lesions and disappearance of all non-target lesions. PR: $\geq 30\%$ decrease in sum of diameters of target lesions, compared to the sum at baseline. The short axis was used in the sum for target nodes, while the longest diameter was used in the sum for all other target lesions. Full analysis set included all enrolled subjects regardless of the treatment received.

End point type	Secondary
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End point timeframe:

From Day 28 of cycle 1 up to Day 14 of cycle 18

End point values	Part A: Sunitinib 15 mg/m ²	Part A: Sunitinib 20 mg/m ²	Part B: Sunitinib 15 mg/m ²	Part B: Sunitinib 20 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	8	3
Units: Percentage of subjects				
number (confidence interval 95%)				
CR + PR	0 (0.0 to 45.9)	0 (0.0 to 45.9)	0 (0.0 to 36.9)	0 (0.0 to 70.8)

End point values	Part C: Sunitinib 15 mg/m ²			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Percentage of subjects				
number (confidence interval 95%)				
CR + PR	0 (0.0 to 26.5)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 30 days after last dose of study drug (maximum duration: Part A: 4 cycles, Part B: 9 cycles, Part C: 18 cycles)

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 subject and as nonserious in another subject, or one subject may have experienced both a serious and nonserious event during the study.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	15.1
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Reporting groups

Reporting group title	Part A: Sunitinib 15 mg/m ²
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Reporting group description:

Subjects with recurrent or refractory solid tumour received 15 mg/m² of sunitinib orally, once daily for 28 days in each cycle of 42 days.

Reporting group title	Part A: Sunitinib 20 mg/m ²
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Reporting group description:

Subjects with recurrent or refractory solid tumour received 20 mg/m² of sunitinib orally, once daily for 28 days in each cycle of 42 days.

Reporting group title	Part B: Sunitinib 15 mg/m ²
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Reporting group description:

Subjects with recurrent or refractory solid tumour received 15 mg/m² of sunitinib orally, once daily for 28 days in each cycle of 42 days.

Reporting group title	Part B: Sunitinib 20 mg/m ²
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Reporting group description:

Subjects with recurrent or refractory solid tumour received 20 mg/m² of sunitinib orally, once daily for 28 days in each cycle of 42 days.

Reporting group title	Part C: Sunitinib 15 mg/m ²
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Reporting group description:

Subjects with recurrent or refractory solid tumour received 15 mg/m² of sunitinib orally, once daily for 28 days in each cycle of 42 days.

Serious adverse events	Part A: Sunitinib 15 mg/m ²	Part A: Sunitinib 20 mg/m ²	Part B: Sunitinib 15 mg/m ²
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 6 (50.00%)	3 / 6 (50.00%)	3 / 8 (37.50%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Shunt malfunction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			

subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular dysfunction			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Convulsion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depressed level of consciousness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glossopharyngeal nerve disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vagus nerve disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral motor neuropathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flatulence			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumatosis intestinalis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspiration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 6 (0.00%)	2 / 6 (33.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperuricaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophosphataemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part B: Sunitinib 20 mg/m ²	Part C: Sunitinib 15 mg/m ²	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	6 / 12 (50.00%)	
number of deaths (all causes)	1	2	
number of deaths resulting from adverse events	0	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Shunt malfunction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			

subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular dysfunction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depressed level of consciousness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glossopharyngeal nerve disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vagus nerve disorder			
subjects affected / exposed	1 / 3 (33.33%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral motor neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 3 (0.00%)	3 / 12 (25.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
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 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flatulence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumatosis intestinalis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
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 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspiration			
subjects affected / exposed	2 / 3 (66.67%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperuricaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Part A: Sunitinib 15 mg/m ²	Part A: Sunitinib 20 mg/m ²	Part B: Sunitinib 15 mg/m ²
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	6 / 6 (100.00%)	8 / 8 (100.00%)
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	3 / 8 (37.50%)
occurrences (all)	0	0	9
Hypotension			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
General disorders and administration site conditions			
Chills			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Death			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Face oedema			

subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	3 / 6 (50.00%)	1 / 6 (16.67%)	2 / 8 (25.00%)
occurrences (all)	4	1	2
Gait disturbance			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Ill-defined disorder			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Pain			
subjects affected / exposed	2 / 6 (33.33%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	2	0	1
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	1 / 8 (12.50%)
occurrences (all)	1	1	1
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Bronchospasm			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	2 / 6 (33.33%)	2 / 6 (33.33%)	1 / 8 (12.50%)
occurrences (all)	2	2	1
Dyspnoea			

subjects affected / exposed	2 / 6 (33.33%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Epistaxis			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Hypoxia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	2 / 6 (33.33%)	1 / 8 (12.50%)
occurrences (all)	0	2	1
Pleural effusion			
subjects affected / exposed	2 / 6 (33.33%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Respiratory disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0

Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Alanine aminotransferase increased			
subjects affected / exposed	2 / 6 (33.33%)	2 / 6 (33.33%)	2 / 8 (25.00%)
occurrences (all)	2	3	6
Amylase increased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 6 (33.33%)	1 / 8 (12.50%)
occurrences (all)	0	2	1
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 6 (50.00%)	4 / 6 (66.67%)	3 / 8 (37.50%)
occurrences (all)	3	6	4
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 6 (33.33%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Blood antidiuretic hormone abnormal			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Blood cholesterol increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Blood thyroid stimulating hormone			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Blood urea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram QT prolonged			

subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Lipase increased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 6 (33.33%)	2 / 8 (25.00%)
occurrences (all)	0	2	2
Lymphocyte count decreased			
subjects affected / exposed	4 / 6 (66.67%)	2 / 6 (33.33%)	2 / 8 (25.00%)
occurrences (all)	7	2	2
Neutrophil count decreased			
subjects affected / exposed	3 / 6 (50.00%)	5 / 6 (83.33%)	4 / 8 (50.00%)
occurrences (all)	4	7	12
Platelet count decreased			
subjects affected / exposed	5 / 6 (83.33%)	4 / 6 (66.67%)	0 / 8 (0.00%)
occurrences (all)	5	6	0
Weight decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
White blood cell count decreased			
subjects affected / exposed	4 / 6 (66.67%)	5 / 6 (83.33%)	3 / 8 (37.50%)
occurrences (all)	5	7	12
Blood bilirubin increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Injury			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Wound			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	1 / 8 (12.50%) 1
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Left ventricular dysfunction			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Ataxia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	6
Droping			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Dysgeusia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Facial nerve disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Glossopharyngeal nerve disorder			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Head discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 6 (0.00%)	2 / 6 (33.33%)	2 / 8 (25.00%)
occurrences (all)	0	2	2
Hemiparesis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Hydrocephalus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
IIIrd nerve disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Nervous system disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nystagmus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Peripheral motor neuropathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Pyramidal tract syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Tremor			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
VIth nerve disorder			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0
Vagus nerve disorder subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	3 / 6 (50.00%) 5	2 / 6 (33.33%) 2	2 / 8 (25.00%) 5
Ear and labyrinth disorders External ear pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0
Eye disorders Extraocular muscle paresis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0
Eye swelling subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0
Lacrimation increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	0 / 8 (0.00%) 0
Vision blurred subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	1 / 8 (12.50%) 2
Visual impairment subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0
Gastrointestinal disorders Abdominal distension subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0
Abdominal pain subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2	0 / 6 (0.00%) 0	1 / 8 (12.50%) 1
Abdominal pain upper			

subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Constipation			
subjects affected / exposed	3 / 6 (50.00%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	3	0	2
Diarrhoea			
subjects affected / exposed	3 / 6 (50.00%)	1 / 6 (16.67%)	3 / 8 (37.50%)
occurrences (all)	3	1	3
Dyspepsia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Gingival pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	3 / 6 (50.00%)	2 / 6 (33.33%)	2 / 8 (25.00%)
occurrences (all)	3	2	4
Proctalgia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Rectal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Small intestinal obstruction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	1 / 6 (16.67%)	2 / 6 (33.33%)	1 / 8 (12.50%)
occurrences (all)	1	2	1
Vomiting			
subjects affected / exposed	2 / 6 (33.33%)	3 / 6 (50.00%)	3 / 8 (37.50%)
occurrences (all)	3	3	3
Hepatobiliary disorders			

Cholelithiasis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Erythema multiforme			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Onychomadesis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Pain of skin			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Purpura			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	1 / 8 (12.50%) 1
Skin discolouration subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0
Skin hypopigmentation subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 2	2 / 8 (25.00%) 2
Renal and urinary disorders			
Chromaturia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0
Dysuria subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0
Haematuria subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	1 / 8 (12.50%) 2
Haemoglobinuria subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0
Proteinuria subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 6 (16.67%) 1	0 / 8 (0.00%) 0
Urinary retention subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0
Endocrine disorders			
Hyperthyroidism subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0
Hypothyroidism subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	1 / 8 (12.50%) 2
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	1 / 8 (12.50%)
occurrences (all)	1	1	4
Back pain			
subjects affected / exposed	2 / 6 (33.33%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	3	0	1
Joint effusion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Muscular weakness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Cystitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Lip infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Sinusitis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	1 / 8 (12.50%)
occurrences (all)	0	2	1
Decreased appetite			
subjects affected / exposed	2 / 6 (33.33%)	1 / 6 (16.67%)	0 / 8 (0.00%)
occurrences (all)	2	1	0
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Hypercalcaemia			
subjects affected / exposed	4 / 6 (66.67%)	1 / 6 (16.67%)	0 / 8 (0.00%)
occurrences (all)	5	1	0
Hyperglycaemia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	1 / 8 (12.50%)
occurrences (all)	1	1	1
Hyperkalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	3
Hypermagnesaemia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	1 / 8 (12.50%)
occurrences (all)	1	1	1
Hypernatraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	4
Hypertriglyceridaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Hyperuricaemia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	1 / 8 (12.50%) 1
Hypoalbuminaemia subjects affected / exposed occurrences (all)	3 / 6 (50.00%) 3	2 / 6 (33.33%) 2	0 / 8 (0.00%) 0
Hypocalcaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0
Hypochloraemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0
Hypoglycaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	2 / 6 (33.33%) 2	0 / 8 (0.00%) 0
Hypokalaemia subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2	1 / 6 (16.67%) 1	0 / 8 (0.00%) 0
Hypomagnesaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	1 / 8 (12.50%) 1
Hyponatraemia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 6 (16.67%) 1	0 / 8 (0.00%) 0
Hypophosphataemia subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2	1 / 6 (16.67%) 1	4 / 8 (50.00%) 5

Non-serious adverse events	Part B: Sunitinib 20 mg/m ²	Part C: Sunitinib 15 mg/m ²	
Total subjects affected by non-serious adverse events subjects affected / exposed	3 / 3 (100.00%)	12 / 12 (100.00%)	
Vascular disorders Flushing subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	
Hypertension			

subjects affected / exposed	2 / 3 (66.67%)	5 / 12 (41.67%)	
occurrences (all)	2	10	
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Death			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Face oedema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)	8 / 12 (66.67%)	
occurrences (all)	1	12	
Gait disturbance			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Ill-defined disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Pyrexia			

subjects affected / exposed	0 / 3 (0.00%)	3 / 12 (25.00%)	
occurrences (all)	0	4	
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Bronchospasm			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Cough			
subjects affected / exposed	1 / 3 (33.33%)	2 / 12 (16.67%)	
occurrences (all)	1	3	
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	1 / 3 (33.33%)	2 / 12 (16.67%)	
occurrences (all)	1	2	
Hypoxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Respiratory disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Rhinitis allergic			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Psychiatric disorders			

Agitation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	3 / 12 (25.00%)	
occurrences (all)	0	4	
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Alanine aminotransferase increased			
subjects affected / exposed	1 / 3 (33.33%)	6 / 12 (50.00%)	
occurrences (all)	1	13	
Amylase increased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 3 (33.33%)	3 / 12 (25.00%)	
occurrences (all)	2	3	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	3 / 12 (25.00%)	
occurrences (all)	0	4	
Blood antidiuretic hormone abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Blood cholesterol increased			

subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	3
Blood creatinine increased		
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)
occurrences (all)	1	2
Blood thyroid stimulating hormone		
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	1
Blood thyroid stimulating hormone increased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0
Blood urea		
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0
Electrocardiogram QT prolonged		
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	1
Gamma-glutamyltransferase increased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0
Lipase increased		
subjects affected / exposed	0 / 3 (0.00%)	3 / 12 (25.00%)
occurrences (all)	0	3
Lymphocyte count decreased		
subjects affected / exposed	1 / 3 (33.33%)	6 / 12 (50.00%)
occurrences (all)	1	12
Neutrophil count decreased		
subjects affected / exposed	0 / 3 (0.00%)	6 / 12 (50.00%)
occurrences (all)	0	20
Platelet count decreased		
subjects affected / exposed	0 / 3 (0.00%)	4 / 12 (33.33%)
occurrences (all)	0	13
Weight decreased		

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	
White blood cell count decreased subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	6 / 12 (50.00%) 24	
Blood bilirubin increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	
Injury, poisoning and procedural complications			
Contusion subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	
Injury subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	
Wound subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	
Cardiac disorders			
Cardiac arrest subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	
Left ventricular dysfunction subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	
Sinus bradycardia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	
Sinus tachycardia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	3 / 12 (25.00%) 3	
Nervous system disorders			
Aphasia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	2 / 12 (16.67%) 3	
Ataxia			

subjects affected / exposed	2 / 3 (66.67%)	3 / 12 (25.00%)
occurrences (all)	2	3
Dizziness		
subjects affected / exposed	0 / 3 (0.00%)	3 / 12 (25.00%)
occurrences (all)	0	4
Drooling		
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0
Dysgeusia		
subjects affected / exposed	0 / 3 (0.00%)	3 / 12 (25.00%)
occurrences (all)	0	3
Facial nerve disorder		
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	2
Glossopharyngeal nerve disorder		
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	2
Head discomfort		
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	2
Headache		
subjects affected / exposed	1 / 3 (33.33%)	4 / 12 (33.33%)
occurrences (all)	1	8
Hemiparesis		
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	1
Hydrocephalus		
subjects affected / exposed	1 / 3 (33.33%)	0 / 12 (0.00%)
occurrences (all)	1	0
IIIrd nerve disorder		
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0
Nervous system disorder		
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	1
Nystagmus		

subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Peripheral motor neuropathy			
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	
occurrences (all)	1	2	
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Pyramidal tract syndrome			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
VIth nerve disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Vagus nerve disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 3 (33.33%)	6 / 12 (50.00%)	
occurrences (all)	1	17	
Ear and labyrinth disorders			
External ear pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Eye disorders			
Extraocular muscle paresis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Eye swelling			
subjects affected / exposed	1 / 3 (33.33%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Lacrimation increased			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	
Vision blurred subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	3 / 12 (25.00%) 3	
Visual impairment subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	
Gastrointestinal disorders			
Abdominal distension subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	
Abdominal pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	3 / 12 (25.00%) 3	
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	
Constipation subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 2	3 / 12 (25.00%) 3	
Diarrhoea subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	3 / 12 (25.00%) 3	
Dyspepsia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	
Dysphagia subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 12 (0.00%) 0	
Gingival pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 2	
Nausea subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	4 / 12 (33.33%) 5	

Proctalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Small intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	4 / 12 (33.33%)	
occurrences (all)	0	5	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Dermatitis acneiform			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Dry skin			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Erythema multiforme			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Hyperhidrosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Onychomadesis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Pain of skin			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Purpura			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Rash maculo-papular			
subjects affected / exposed	1 / 3 (33.33%)	2 / 12 (16.67%)	
occurrences (all)	1	3	
Skin discolouration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Skin hypopigmentation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Haemoglobinuria			

subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	2	
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	10	
Urinary retention			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Hypothyroidism			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	1 / 3 (33.33%)	2 / 12 (16.67%)	
occurrences (all)	1	3	
Joint effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	2	
Myalgia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Neck pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Pain in extremity			

subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	1 / 12 (8.33%) 1	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Cystitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Lip infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Skin infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	1 / 3 (33.33%)	2 / 12 (16.67%)	
occurrences (all)	1	3	
Decreased appetite			
subjects affected / exposed	2 / 3 (66.67%)	1 / 12 (8.33%)	
occurrences (all)	2	1	
Dehydration			
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Hypercalcaemia			

subjects affected / exposed	0 / 3 (0.00%)	5 / 12 (41.67%)
occurrences (all)	0	8
Hyperglycaemia		
subjects affected / exposed	1 / 3 (33.33%)	4 / 12 (33.33%)
occurrences (all)	1	7
Hyperkalaemia		
subjects affected / exposed	1 / 3 (33.33%)	3 / 12 (25.00%)
occurrences (all)	1	3
Hypermagnesaemia		
subjects affected / exposed	1 / 3 (33.33%)	6 / 12 (50.00%)
occurrences (all)	1	9
Hypernatraemia		
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	1
Hypertriglyceridaemia		
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	3
Hyperuricaemia		
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	2
Hypoalbuminaemia		
subjects affected / exposed	1 / 3 (33.33%)	2 / 12 (16.67%)
occurrences (all)	1	2
Hypocalcaemia		
subjects affected / exposed	0 / 3 (0.00%)	4 / 12 (33.33%)
occurrences (all)	0	7
Hypochloraemia		
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	2
Hypoglycaemia		
subjects affected / exposed	0 / 3 (0.00%)	3 / 12 (25.00%)
occurrences (all)	0	3
Hypokalaemia		
subjects affected / exposed	1 / 3 (33.33%)	4 / 12 (33.33%)
occurrences (all)	2	8
Hypomagnesaemia		

subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	3	
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	3 / 12 (25.00%)	
occurrences (all)	0	8	
Hypophosphataemia			
subjects affected / exposed	1 / 3 (33.33%)	2 / 12 (16.67%)	
occurrences (all)	1	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 March 2008	1.The study was amended due to cardiac toxicity of sunitinib to exclude subjects who were previously treated with potentially cardiotoxic therapies including anthracyclines or radiotherapy involving the heart. 2.Subjects with CNS tumors were allowed to enroll on study. 3.Updated Comprehensive Adverse Events and Potential Risks (CAEPR) for sunitinib and additional potential surrogate biomarkers related to angiogenesis.
25 February 2009	The CAEPR version was updated. The risks section of the informed consent was also updated to match those described in the new CAEPR.
28 December 2009	A new Part (Part C) was added to the study to evaluate the PK of sunitinib when the capsule contents were sprinkled over applesauce or yogurt. The sunitinib dose administered in this component of the trial was the RP2D of 15 mg/m ² /day given orally once daily. The background section had been modified to describe the rationale for this amendment.
08 March 2010	The Language added to the protocol and the informed consent addressing risks to the caregiver preparing the powder formulation of sunitinib. Since the risks of sunitinib to an unborn baby were not known, pregnant women should have not prepared the sunitinib.
06 October 2010	Eligibility criteria was clarified in the protocol to limit enrollment to subjects with solid tumors or CNS tumors without imaging evidence of current or prior intracranial hemorrhage on appropriate MRI imaging sequences.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported