# 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 |

**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) | EMEA-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/m^2) 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/m^2 capsule of sunitinib based on the body surface area (BSA) once daily.

| | |
|---|---|
| **Arm title** | Part A: Sunitinib 20 mg/m^2 |

Arm 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.

| | |
|---|---|
| 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 B: Sunitinib 15 mg/m^2 |

Arm 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.

| | |
|---|---|
| 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/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/m^2 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/m^2 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<br>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-hemotologic 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 transminase, alanine transminase and biluribin (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/m^2 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 /m^2.

| 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) |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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*10^3/millimeter[mm]^3,g2:

<75*10^3/mm^3 to 50*10^3/mm^3,g3:<50*10^3/mm^3 to 25*10^3/mm^3,g4:<25*10^3/mm^3); white blood cell count (WBC)(g1:<LLN to 3*10^3/mm^3,g2:<3*10^3 to 2*10^3/mm^3,g3:<2*10^3 to 1*10^3/mm^3,g4:<1*10^3/mm^3); 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 |
|---|---|

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] |
|---|---|

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/m^2 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 |
|---|---|

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/m^2 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 (± 54) | 99999 (± 99999) | 3.45750 (± 102) | 1.755 (± 13249) |

## 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] |
|---|---|

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/m^2 arm was not evaluable as the plasma concentration for this arm at the pre-specified time points was 0.

| End point type | Secondary |
|---|---|

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/m^2 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] |
|---|---|

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/m^2 arm was not evaluable as the plasma concentration for this arm at the pre-specified time points was 0.

| End point type | Secondary |
|---|---|

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/m^2 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] |
|---|---|

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/m^2 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 |
|---|---|

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/m^2 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] |
|---|---|

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/m^2 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 |
|---|---|

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/m^2 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] |
|---|---|

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/m^2 arm was not evaluable as the plasma concentration for this arm at the pre-specified time points was 0.

| End point type | Secondary |
|---|---|

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/m^2 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] |
|---|---|

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/m^2 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 |
|---|---|

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/m^2 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 (t1/2) of Sunitinib and its metabolite

| End point title | Terminal Elimination Half-Life (t1/2) of Sunitinib and its metabolite[9] |
|---|---|

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/m^2 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 |
|---|---|

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/m^2 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 |
|---|---|

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: >= 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 |
|---|---|

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 |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 15.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Part A: 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 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.

| 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 | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all) | 0 | 0 | 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 |
| Drooling | | | |
| 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 | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vagus nerve disorder | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 3 / 6 (50.00%) | 2 / 6 (33.33%) | 2 / 8 (25.00%) |
| occurrences (all) | 5 | 2 | 5 |
| Ear and labyrinth disorders | | | |
| External ear pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |
| Extraocular muscle paresis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye swelling | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lacrimation increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 6 (16.67%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all) | 0 | 0 | 2 |
| Visual impairment | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 6 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 6 (33.33%) | 0 / 6 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all) | 2 | 0 | 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 | 0 / 6 (0.00%) | 1 / 6 (16.67%) | 1 / 8 (12.50%) |
| occurrences (all) | 0 | 1 | 1 |
| Skin discolouration | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 6 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin hypopigmentation | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 6 (16.67%) | 2 / 8 (25.00%) |
| occurrences (all) | 0 | 2 | 2 |
| Renal and urinary disorders | | | |
| Chromaturia | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 6 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dysuria | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematuria | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 6 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all) | 1 | 0 | 2 |
| Haemoglobinuria | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Proteinuria | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 6 (16.67%) | 0 / 8 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Endocrine disorders | | | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 6 (16.67%) | 1 / 8 (12.50%) |
| occurrences (all) | 0 | 1 | 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 | 1 / 6 (16.67%) | 0 / 6 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all) | 1 | 0 | 1 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 3 / 6 (50.00%) | 2 / 6 (33.33%) | 0 / 8 (0.00%) |
| occurrences (all) | 3 | 2 | 0 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypochloraemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 6 (33.33%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 2 / 6 (33.33%) | 1 / 6 (16.67%) | 0 / 8 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 6 (16.67%) | 1 / 8 (12.50%) |
| occurrences (all) | 0 | 1 | 1 |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 6 (16.67%) | 0 / 8 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 2 / 6 (33.33%) | 1 / 6 (16.67%) | 4 / 8 (50.00%) |
| occurrences (all) | 2 | 1 | 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 | 0 / 3 (0.00%) | 1 / 12 (8.33%) | |
| occurrences (all) | 0 | 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 | 0 / 3 (0.00%) | 0 / 12 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 6 / 12 (50.00%) | |
| occurrences (all) | 1 | 24 | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 12 (8.33%) | |
| occurrences (all) | 0 | 1 | |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 12 (8.33%) | |
| occurrences (all) | 0 | 1 | |
| Injury | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 12 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Wound | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 12 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Cardiac disorders | | | |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 12 (8.33%) | |
| occurrences (all) | 0 | 1 | |
| Left ventricular dysfunction | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 12 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Sinus bradycardia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 12 (8.33%) | |
| occurrences (all) | 0 | 1 | |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 3 / 12 (25.00%) | |
| occurrences (all) | 0 | 3 | |
| Nervous system disorders | | | |
| Aphasia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 12 (16.67%) | |
| occurrences (all) | 0 | 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 | 0 / 3 (0.00%) | 0 / 12 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 3 / 12 (25.00%) | |
| occurrences (all) | 0 | 3 | |
| Visual impairment | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 12 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 12 (8.33%) | |
| occurrences (all) | 0 | 1 | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 3 / 12 (25.00%) | |
| occurrences (all) | 0 | 3 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 12 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Constipation | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 3 / 12 (25.00%) | |
| occurrences (all) | 2 | 3 | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 3 / 12 (25.00%) | |
| occurrences (all) | 1 | 3 | |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 12 (8.33%) | |
| occurrences (all) | 0 | 1 | |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 12 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Gingival pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 12 (8.33%) | |
| occurrences (all) | 0 | 2 | |
| Nausea | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 4 / 12 (33.33%) | |
| occurrences (all) | 0 | 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 | 1 / 3 (33.33%) | 1 / 12 (8.33%) | |
| occurrences (all) | 1 | 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.<br>2.Subjects with CNS tumors were allowed to enroll on study.<br>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