# Clinical trial results:
# Axitinib (AG-013736) As Second Line Therapy For Metastatic Renal Cell Cancer: Axis Trial

## Summary

| | |
|---|---|
| EudraCT number | 2008-001451-21 |
| Trial protocol | SE ES AT FR GB IE DE IT PL GR SK |
| Global end of trial date | 25 February 2016 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 16 March 2017 |
| First version publication date | 16 March 2017 |
| Summary attachment (see zip file) | A4061032 EU Posting (A4061032 PDS.pdf) |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | A4061032 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00678392 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Pfizer, Inc. |
| Sponsor organisation address | 235 E 42nd Street, New York, United States, NY 10017 |
| Public contact | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com |

Notes:

**Paediatric regulatory details**

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

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 09 June 2016 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 25 February 2016 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

Compare the progression-free survival (PFS) of subjects with mRCC receiving AG-013736 vs sorafenib following failure of one prior systemic first-line regimen containing one or more of the following: sunitinib, bevacizumab + IFN alpha, temsirolimus, or cytokine(s).

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 trials subjects were followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 03 September 2008 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Australia: 11 |
| Country: Number of subjects enrolled | Austria: 6 |
| Country: Number of subjects enrolled | Brazil: 17 |
| Country: Number of subjects enrolled | Canada: 17 |
| Country: Number of subjects enrolled | China: 26 |
| Country: Number of subjects enrolled | France: 67 |
| Country: Number of subjects enrolled | Germany: 22 |
| Country: Number of subjects enrolled | Greece: 4 |
| Country: Number of subjects enrolled | India: 23 |
| Country: Number of subjects enrolled | Ireland: 2 |
| Country: Number of subjects enrolled | Italy: 40 |
| Country: Number of subjects enrolled | Japan: 54 |
| Country: Number of subjects enrolled | Korea, Republic of: 25 |
| Country: Number of subjects enrolled | Poland: 56 |
| Country: Number of subjects enrolled | Russian Federation: 81 |
| Country: Number of subjects enrolled | Singapore: 4 |
| Country: Number of subjects enrolled | Slovakia: 7 |
| Country: Number of subjects enrolled | Spain: 21 |
| Country: Number of subjects enrolled | Sweden: 3 |

| | |
|---|---|
| Country: Number of subjects enrolled | Taiwan: 20 |
| Country: Number of subjects enrolled | United Kingdom: 48 |
| Country: Number of subjects enrolled | United States: 169 |
| Worldwide total number of subjects | 723 |
| EEA total number of subjects | 276 |

Notes:

**Subjects enrolled per age group**

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 476 |
| From 65 to 84 years | 247 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

This study was conducted at multiple sites in United Kingdom. Study started on 03 September 2008 and completed on 25 February 2016.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Axitinib 5 mg |

Arm description:

Axitinib (AG-013736) 5 milligram (mg) tablet administered orally twice daily in cycles of 4 weeks.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Axitinib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received Axitinib (AG-013736) 5 mg tablet orally twice daily in cycles of 4 weeks.

| | |
|---|---|
| **Arm title** | Sorafenib 400 mg |

Arm description:

Sorafenib 400 mg tablet administered orally twice daily in cycles of 4 weeks.

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Sorafenib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received Sorafenib 400 mg tablet orally twice daily in cycles of 4 weeks.

| **Number of subjects in period 1** | Axitinib 5 mg | Sorafenib 400 mg |
|---|---|---|
| Started | 361 | 362 |
| Completed | 0 | 0 |
| Not completed | 361 | 362 |
| Consent withdrawn by subject | 4 | 4 |
| Adverse Event | - | 6 |

| | | |
|---|---|---|
| Objective Progression or Relapse | 3 | 8 |
| Death | 280 | 269 |
| Sponsor Decision | 1 | 2 |
| Randomized But Not Treated | 2 | 7 |
| Unspecified | 56 | 53 |
| Lost to follow-up | 15 | 13 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Axitinib 5 mg |
| Reporting group description: | |
| Axitinib (AG-013736) 5 milligram (mg) tablet administered orally twice daily in cycles of 4 weeks. | |
| Reporting group title | Sorafenib 400 mg |
| Reporting group description: | |
| Sorafenib 400 mg tablet administered orally twice daily in cycles of 4 weeks. | |

| Reporting group values | Axitinib 5 mg | Sorafenib 400 mg | Total |
|---|---|---|---|
| Number of subjects | 361 | 362 | 723 |
| Age Categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 238 | 238 | 476 |
| From 65-84 years | 123 | 124 | 247 |
| Age Continuous<br>Units: years | | | |
| arithmetic mean | 59.7 | 60 | |
| standard deviation | ± 10.5 | ± 10.1 | - |
| Gender Categorical<br>Units: Subjects | | | |
| Female | 96 | 104 | 200 |
| Male | 265 | 258 | 523 |

## End points

| End points reporting groups | |
|---|---|
| Reporting group title | Axitinib 5 mg |
| Reporting group description: | |
| Axitinib (AG-013736) 5 milligram (mg) tablet administered orally twice daily in cycles of 4 weeks. | |
| Reporting group title | Sorafenib 400 mg |
| Reporting group description: | |
| Sorafenib 400 mg tablet administered orally twice daily in cycles of 4 weeks. | |

| Primary: Progression-Free Survival (PFS) | |
|---|---|
| End point title | Progression-Free Survival (PFS) |
| End point description: | |
| PFS was defined as the time in months from start of study treatment to the first documentation of objective tumor progression of disease (PD) or to death due to any cause, whichever occurs first. PD was assessed by response evaluation criteria in solid tumors (RECIST) version 1.0. PD = greater than or equal to (>=) 20 percent (%) increase in the sum of the longest dimensions (LD) of the target lesions taking as a reference the smallest sum of the LD recorded since the start of treatment or unequivocal progression in non-target lesions or the appearance of 1 or more new lesions. Occurrence of a pleural effusion or ascites was also considered PD if demonstrated by cytological investigation and it was not previously documented. New bone lesions not previously documented were considered PD if confirmed by computed tomography/magnetic resonance imaging or X-ray. Full analysis set (FAS). | |
| End point type | Primary |
| End point timeframe: | |
| From initiation of treatment up to follow-up period (up to 3 years) | |

| End point values | Axitinib 5 mg | Sorafenib 400 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 361 | 362 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 6.7 (6.3 to 8.6) | 4.7 (4.6 to 5.6) | | |

### Statistical analyses

| Statistical analysis title | Axitinib vs Sorafenib |
|---|---|
| Comparison groups | Sorafenib 400 mg v Axitinib 5 mg |
| Number of subjects included in analysis | 723 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [1] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.665 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.544 |
| upper limit | 0.812 |

Notes:

[1] - P-value was obtained from 1-sided log rank test, stratified by eastern cooperative oncology group (ECOG) and prior treatment. One-sided log-rank test at 0.025 level of significance was used to compare PFS between the 2 treatment arms.

## Secondary: Overall Survival (OS)

| | |
|---|---|
| End point title | Overall Survival (OS) |

End point description:

Overall survival was defined as the duration from start of study treatment to date of death due to any cause. OS was calculated as (months) = (date of death minus the date of first dose of study medication plus 1) divided by 30.4. For subjects who were alive, overall survival was censored on last date the subjects were known to be alive. FAS included all subjects who were randomized, with study drug assignment designated according to initial randomization, regardless of whether subjects received study drug or receive a different drug from that to which they were randomized.

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

End point timeframe:

From initiation of treatment up to follow-up period (up to 3 years)

| **End point values** | Axitinib 5 mg | Sorafenib 400 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 361 | 362 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 20.1 (16.7 to 23.4) | 19.2 (17.5 to 22.3) | | |

### Statistical analyses

| **Statistical analysis title** | Axitinib vs Sorafenib |
|---|---|
| Comparison groups | Axitinib 5 mg v Sorafenib 400 mg |
| Number of subjects included in analysis | 723 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3744 [2] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.969 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.8 |
| upper limit | 1.174 |

Notes:

[2] - P-value was obtained from a 1-sided log-rank test of treatment stratified by ECOG performance status and prior treatment.

## Secondary: Objective Response Rate (ORR)

| End point title | Objective Response Rate (ORR) |
|---|---|

End point description:

ORR = percentage of subjects with confirmed complete response (CR) or confirmed partial response (PR) according to the RECIST version 1.0 recorded from first dose of study treatment until PD or death due to any cause. CR: disappearance of all target, non target lesions and no appearance of new lesions, documented on 2 occasions separated by at least 4 weeks. PR: at least 30 % decrease in sum of LD of target lesions taking as reference baseline sum of LD, without progression of non target lesions, no appearance of new lesions. PD: >=20% increase in sum of LD of the target lesions taking as a reference smallest sum of LD recorded since the start of treatment or unequivocal progression in non-target lesions or appearance of 1 or more new lesions. Occurrence of pleural effusion or ascites if demonstrated by cytological investigation, not previously documented. New bone lesions not previously documented if confirmed by computed tomography/magnetic resonance imaging or X-ray. FAS.

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

End point timeframe:

From initiation of treatment up to follow-up period (up to 3 years)

| **End point values** | Axitinib 5 mg | Sorafenib 400 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 361 | 362 | | |
| Units: Percentage of Subjects | | | | |
| number (confidence interval 95%) | 19.4 (15.4 to 23.9) | 9.4 (6.6 to 12.9) | | |

### Statistical analyses

| **Statistical analysis title** | Axitinib vs Sorafenib |
|---|---|
| Comparison groups | Axitinib 5 mg v Sorafenib 400 mg |
| Number of subjects included in analysis | 723 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0001 [3] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 2.056 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.408 |
| upper limit | 3.003 |

Notes:

[3] - P-value was obtained from a 1-sided Cochran-Mantel-Haenszel test of treatment stratified by ECOG performance status and prior treatment.

## Secondary: Duration of Response (DR)

| End point title | Duration of Response (DR) |
|---|---|

End point description:

DR: time from first documentation of objective tumor response (CR or PR), that was subsequently confirmed, to first documentation of PD or to death due to any cause, whichever occurred first as per RECIST version 1.0, a) CR: disappearance of all target, non target lesions and no appearance of new lesions, documented on 2 occasions separated by at least 4 weeks, b) PR: at least 30 % decrease in sum of LD of target lesions taking as reference baseline sum of LD, without progression of non target lesions, no appearance of new lesions, c) PD: >=20% increase in sum of LD of the target lesions taking as a reference smallest sum of LD recorded since the start of treatment or unequivocal progression in non-target lesions or appearance of 1 or more new lesions. Occurrence of pleural effusion or ascites if demonstrated by cytological investigation, not previously documented. New bone lesions not previously documented if confirmed by computed tomography/magnetic resonance imaging or X-ray. FAS.

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

End point timeframe:

From initiation of treatment up to follow-up period (up to 3 years)

| **End point values** | Axitinib 5 mg | Sorafenib 400 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 361[4] | 362 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 11 (7.4 to 99999) | 10.6 (8.8 to 11.5) | | |

Notes:

[4] - 99999: upper limit of 95% confidence interval was not reached at time of data cut-off.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects With Treatment-Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs)

| End point title | Percentage 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 study drug 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. A treatment emergent AE was defined as an event that emerged during the treatment period that was absent before treatment, or worsened during the treatment period relative to the pretreatment state. AEs included both serious and nonserious AEs. Safety population included all subjects who received at least 1 dose of study medication with treatment assignments designated according to actual study treatment received.

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

End point timeframe:

From initiation of treatment up to follow-up period (up to 3 years)

| End point values | Axitinib 5 mg | Sorafenib 400 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 359 | 355 | | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |
| AEs | 96.1 | 98 | | |
| SAEs | 40.7 | 35.8 | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With Adverse Events (AEs) by Severity

| End point title | Percentage of Subjects With Adverse Events (AEs) by 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. Severity of the AEs was graded according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 3.0. Grade 1= mild; Grade 2= moderate; Grade 3= severe; Grade 4= life-threatening or disabling; Grade 5= death related to AE. Safety population included all subjects who received at least 1 dose of study medication with treatment assignments designated according to actual study treatment received.

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

End point timeframe:

From initiation of treatment up to follow-up period (up to 3 years)

| End point values | Axitinib 5 mg | Sorafenib 400 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 359 | 355 | | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |
| Grade 1 | 3.9 | 3.1 | | |
| Grade 2 | 20.1 | 21.7 | | |
| Grade 3 | 47.6 | 52.4 | | |
| Grade 4 | 10.6 | 11.5 | | |
| Grade 5 | 13.9 | 9.3 | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With Treatment-Related Adverse Events (AEs) and Serious Adverse Events (SAEs)

| End point title | Percentage of Subjects With Treatment-Related Adverse Events (AEs) and Serious Adverse Events (SAEs) |
|---|---|

End point description:

An AE was any untoward medical occurrence attributed to study drug in a subject who received study drug. 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. AEs included both serious and non serious AEs. Safety population included all subjects who received at least 1 dose of study medication with treatment assignments designated according to actual study treatment received.

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

End point timeframe:

From initiation of treatment up to follow-up period (up to 3 years)

| **End point values** | Axitinib 5 mg | Sorafenib 400 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 359 | 355 | | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |
| AEs | 92.2 | 95.2 | | |
| SAEs | 15.3 | 13.8 | | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Number of Subjects With Clinically Significant Laboratory Abnormalities: Hematology**

| End point title | Number of Subjects With Clinically Significant Laboratory Abnormalities: Hematology |
|---|---|

End point description:

Hematology laboratory test included hemoglobin, platelet count, white blood cells count, neutrophils and Lymphocytes. Abnormalities were assessed by CTCAE Grade Version 2 for severity: Grade 1= mild; Grade 2= moderate; Grade 3= severe and Grade 4= life-threatening or disabling. Safety population included all subjects who received at least 1 dose of study medication with treatment assignments designated according to actual study treatment received. Here, "n" signifies number of subjects available for specified categories for each arm respectively.

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

End point timeframe:

From initiation of treatment up to follow-up period (up to 3 years)

| **End point values** | Axitinib 5 mg | Sorafenib 400 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 359 | 355 | | |
| Units: Subjects | | | | |
| number (not applicable) | | | | |
| Hemoglobin: Grade 1 (n =320, 316) | 93 | 112 | | |
| Hemoglobin: Grade 2 (n =320, 316) | 19 | 41 | | |

| | | | | |
|---|---|---|---|---|
| Hemoglobin: Grade 3 (n =320, 316) | 1 | 11 | | |
| Hemoglobin: Grade 4 (n =320, 316) | 0 | 1 | | |
| Lymphocytes: Grade 1 (n =317, 309) | 7 | 7 | | |
| Lymphocytes: Grade 2 (n =317, 309) | 89 | 93 | | |
| Lymphocytes: Grade 3 (n =317, 309) | 10 | 11 | | |
| Lymphocytes: Grade 4 (n =317, 309) | 0 | 0 | | |
| Neutrophils: Grade 1 (n =316, 308) | 13 | 20 | | |
| Neutrophils: Grade 2 (n =316, 308) | 4 | 4 | | |
| Neutrophils: Grade 3 (n =316, 308) | 2 | 2 | | |
| Neutrophils: Grade 4 (n =316, 308) | 0 | 0 | | |
| Platelets: Grade 1 (n =312, 310) | 47 | 41 | | |
| Platelets: Grade 2 (n =312, 310) | 0 | 3 | | |
| Platelets: Grade 3 (n =312, 310) | 1 | 0 | | |
| Platelets: Grade 4 (n =312, 310) | 0 | 0 | | |
| White blood cells: Grade 1 (n =320, 315) | 32 | 36 | | |
| White blood cells: Grade 2 (n =320, 315) | 4 | 12 | | |
| White blood cells: Grade 3 (n =320, 315) | 0 | 1 | | |
| White blood cells: Grade 4 (n =320, 315) | 0 | 0 | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Clinically Significant Laboratory Abnormalities: Biochemistry

| End point title | Number of Subjects With Clinically Significant Laboratory Abnormalities: Biochemistry |
|---|---|

End point description:

Biochemistry laboratory test included parameters: alanine aminotransferase, alkaline phosphatase, amylase, aspartate aminotransferase, bicarbonate, bilirubin, creatinine, hypercalcemia, hyperglycemia, hyperkalemia, hypernatremia, hypoalbuminemia, hypocalcemia, hypoglycemia, hypokalemia, hyponatremia, hypophosphatemia and lipase. Abnormalities were assessed by CTCAE Grade Version 2 for severity: Grade 1= mild; Grade 2= moderate; Grade 3= severe and Grade 4= life-threatening or disabling. Safety population included all subjects who received at least 1 dose of study medication with treatment assignments designated according to actual study treatment received. Here, "n" signifies number of subjects available for specified categories for each arm respectively.

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

End point timeframe:

From initiation of treatment up to follow-up period (up to 3 years)

| End point values | Axitinib 5 mg | Sorafenib 400 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 359 | 355 | | |
| Units: Subjects | | | | |
| number (not applicable) | | | | |
| Alanine aminotransferase: Grade 1 (n =331, 313) | 65 | 57 | | |
| Alanine aminotransferase: Grade 2 (n =331, 313) | 8 | 6 | | |
| Alanine aminotransferase: Grade 3 (n =331, 313) | 1 | 2 | | |
| Alanine aminotransferase: Grade 4 (n =331, 313) | 0 | 3 | | |
| Alkaline phosphatase: Grade 1 (n =336, 319) | 88 | 92 | | |
| Alkaline phosphatase: Grade 2 (n =336, 319) | 8 | 15 | | |
| Alkaline phosphatase: Grade 3 (n =336, 319) | 4 | 3 | | |
| Alkaline phosphatase: Grade 4 (n =336, 319) | 0 | 0 | | |
| Amylase: Grade 1 (n =338, 319) | 64 | 76 | | |
| Amylase: Grade 2 (n =338, 319) | 12 | 21 | | |
| Amylase: Grade 3 (n =338, 319) | 7 | 6 | | |
| Amylase: Grade 4 (n =338, 319) | 0 | 1 | | |
| Aspartate aminotransferase: Grade 1 (n =331, 311) | 59 | 67 | | |
| Aspartate aminotransferase: Grade 2 (n =331, 311) | 5 | 7 | | |
| Aspartate aminotransferase: Grade 3 (n =331, 311) | 1 | 4 | | |
| Aspartate aminotransferase: Grade 4 (n =331, 311) | 0 | 0 | | |
| Bicarbonate: Grade 1 (n =314, 291) | 127 | 115 | | |
| Bicarbonate: Grade 2 (n =314, 291) | 11 | 10 | | |
| Bicarbonate: Grade 3 (n =314, 291) | 0 | 0 | | |
| Bicarbonate: Grade 4 (n =314, 291) | 1 | 0 | | |
| Bilirubin: Grade 1 (n =336, 318) | 16 | 12 | | |
| Bilirubin: Grade 2 (n =336, 318) | 8 | 2 | | |
| Bilirubin: Grade 3 (n =336, 318) | 1 | 1 | | |
| Bilirubin: Grade 4 (n =336, 318) | 0 | 0 | | |
| Creatinine: Grade 1 (n =336, 318) | 155 | 121 | | |
| Creatinine: Grade 2 (n =336, 318) | 30 | 9 | | |
| Creatinine: Grade 3 (n =336, 318) | 0 | 1 | | |
| Creatinine: Grade 4 (n =336, 318) | 0 | 0 | | |
| Hypercalcemia: Grade 1 (n =336, 319) | 92 | 22 | | |
| Hypercalcemia: Grade 2 (n =336, 319) | 8 | 1 | | |
| Hypercalcemia: Grade 3 (n =336, 319) | 1 | 0 | | |
| Hypercalcemia: Grade 4 (n =336, 319) | 0 | 0 | | |
| Hyperglycemia: Grade 1 (n =336, 319) | 41 | 28 | | |
| Hyperglycemia: Grade 2 (n =336, 319) | 45 | 37 | | |
| Hyperglycemia: Grade 3 (n =336, 319) | 7 | 7 | | |
| Hyperglycemia: Grade 4 (n =336, 319) | 0 | 0 | | |
| Hyperkalemia: Grade 1 (n =333, 314) | 0 | 0 | | |
| Hyperkalemia: Grade 2 (n =333, 314) | 42 | 22 | | |

| | | | | |
|---|---|---|---|---|
| Hyperkalemia: Grade 3 (n =333, 314) | 9 | 8 | | |
| Hyperkalemia: Grade 4 (n =333, 314) | 0 | 0 | | |
| Hypernatremia: Grade 1 (n =338, 319) | 34 | 23 | | |
| Hypernatremia: Grade 2 (n =338, 319) | 19 | 14 | | |
| Hypernatremia: Grade 3 (n =338, 319) | 3 | 1 | | |
| Hypernatremia: Grade 4 (n =338, 319) | 0 | 2 | | |
| Hypoalbuminemia: Grade 1 (n =337, 319) | 37 | 25 | | |
| Hypoalbuminemia: Grade 2 (n =337, 319) | 11 | 31 | | |
| Hypoalbuminemia: Grade 3 (n =337, 319) | 1 | 2 | | |
| Hypoalbuminemia: Grade 4 (n =337, 319) | 0 | 0 | | |
| Hypocalcemia: Grade 1 (n =336, 319) | 25 | 67 | | |
| Hypocalcemia: Grade 2 (n =336, 319) | 4 | 18 | | |
| Hypocalcemia: Grade 3 (n =336, 319) | 2 | 2 | | |
| Hypocalcemia: Grade 4 (n =336, 319) | 1 | 2 | | |
| Hypoglycemia: Grade 1 (n =336, 319) | 23 | 9 | | |
| Hypoglycemia: Grade 2 (n =336, 319) | 12 | 16 | | |
| Hypoglycemia: Grade 3 (n =336, 319) | 1 | 1 | | |
| Hypoglycemia: Grade 4 (n =336, 319) | 0 | 0 | | |
| Hypokalemia: Grade 1 (n =333, 314) | 22 | 21 | | |
| Hypokalemia: Grade 2 (n =333, 314) | 0 | 0 | | |
| Hypokalemia: Grade 3 (n =333, 314) | 0 | 5 | | |
| Hypokalemia: Grade 4 (n =333, 314) | 0 | 0 | | |
| Hyponatremia: Grade 1 (n =338, 319) | 33 | 27 | | |
| Hyponatremia: Grade 2 (n =338, 319) | 0 | 0 | | |
| Hyponatremia: Grade 3 (n =338, 319) | 11 | 6 | | |
| Hyponatremia: Grade 4 (n =338, 319) | 1 | 1 | | |
| Hypophosphatemia: Grade 1 (n =336, 318) | 4 | 8 | | |
| Hypophosphatemia: Grade 2 (n =336, 318) | 33 | 99 | | |
| Hypophosphatemia: Grade 3 (n =336, 318) | 6 | 51 | | |
| Hypophosphatemia: Grade 4 (n =336, 318) | 0 | 0 | | |
| Lipase: Grade 1 (n =338, 319) | 53 | 76 | | |
| Lipase: Grade 2 (n =338, 319) | 22 | 25 | | |
| Lipase: Grade 3 (n =338, 319) | 14 | 40 | | |
| Lipase: Grade 4 (n =338, 319) | 2 | 7 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Clinically Significant Laboratory Abnormalities: Urinalysis

| | |
|---|---|
| End point title | Number of Subjects With Clinically Significant Laboratory Abnormalities: Urinalysis |

End point description:

Urinalysis included urine blood/ hemoglobin, glucose and protein. Abnormalities were assessed by CTCAE Grade Version 2 for severity: Grade 1= mild; Grade 2= moderate; Grade 3= severe and Grade 4= life-threatening or disabling. Safety population included all subjects who received at least 1 dose of study medication with treatment assignments designated according to actual study treatment received. Here, "n" signifies number of subjects available for specified categories for each arm respectively.

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

End point timeframe:

From initiation of treatment up to follow-up period (up to 3 years)

| **End point values** | Axitinib 5 mg | Sorafenib 400 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 359 | 355 | | |
| Units: Subjects | | | | |
| number (not applicable) | | | | |
| Urine blood/ hemoglobin: Grade 1 (n =304, 272) | 45 | 35 | | |
| Urine blood/ hemoglobin: Grade 2 (n =304, 272) | 1 | 0 | | |
| Urine blood/ hemoglobin: Grade 3 (n =304, 272) | 0 | 0 | | |
| Urine blood/ hemoglobin: Grade 4 (n =304, 272) | 0 | 0 | | |
| Urine glucose: Grade 1 (n =322, 286) | 12 | 13 | | |
| Urine glucose: Grade 2 (n =322, 286) | 0 | 3 | | |
| Urine glucose: Grade 3 (n =322, 286) | 0 | 0 | | |
| Urine glucose: Grade 4 (n =322, 286) | 1 | 1 | | |
| Urine protein: Grade 1 (n =326, 289) | 105 | 91 | | |
| Urine protein: Grade 2 (n =326, 289) | 31 | 27 | | |
| Urine protein: Grade 3 (n =326, 289) | 27 | 21 | | |
| Urine protein: Grade 4 (n =326, 289) | 9 | 7 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Functional Assessment of Cancer Therapy Kidney Symptom Index-15 (FKSI-15) Score

| End point title | Functional Assessment of Cancer Therapy Kidney Symptom Index-15 (FKSI-15) Score |
|---|---|

End point description:

FKSI was used to assess quality of life (QoL) for those diagnosed with renal cell cancer and consisted of 15 items (lack of energy, side effects, pain, losing weight, bone pain, fatigue, enjoying life, short of breath, worsened condition, appetite, coughing, bothered by fevers, ability to work, hematuria and sleep). Each of the 15 items was answered on a 5-point Likert-type scale ranging from 0 to 4 (0= not at all, 1= a little bit, 2= somewhat, 3= quite a bit, 4= very much). Total FKSI score = sum of the 15 item scores; total range: 0 - 60; 0 (no symptoms) to 60 (very much); higher scores indicate greater presence of symptoms. FAS. Here, "n" signifies those subjects who were evaluable for the specified time points.

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

End point timeframe:

Baseline (Predose on Cycle 1 Day 1) , Day 1 of each cycle until Cycle 21, End of treatment (Day 670) and Follow-up visit (Day 698)

| **End point values** | Axitinib 5 mg | Sorafenib 400 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 361 | 362 | | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n =346, 342) | 43.199 (± 8.416) | 43.339 (± 8.162) | | |
| Cycle 2/Day1 (n =319, 296) | 42.351 (± 8.305) | 41.688 (± 7.696) | | |
| Cycle 3/Day1 (n =279, 246) | 42.59 (± 7.729) | 42.424 (± 7.888) | | |
| Cycle 4/Day1 (n =257, 221) | 42.791 (± 8.18) | 43.424 (± 7.345) | | |
| Cycle 5/Day1 (n =238, 203) | 42.968 (± 8.152) | 42.907 (± 7.255) | | |
| Cycle 6/Day1 (n =213, 179) | 42.949 (± 7.842) | 43.057 (± 7.724) | | |
| Cycle 7/Day1 (n =206, 158) | 42.747 (± 7.621) | 43.578 (± 7.621) | | |
| Cycle 8/Day1 (n =177, 136) | 43.58 (± 7.578) | 44.074 (± 7.757) | | |
| Cycle 9/Day1 (n =163, 118) | 43.191 (± 8.3) | 44.518 (± 6.511) | | |
| Cycle 10/Day1 (n =146, 96) | 43.312 (± 8.564) | 44.771 (± 7.155) | | |
| Cycle 11/Day1 (n =122, 85) | 44.119 (± 8.306) | 44.438 (± 7.388) | | |
| Cycle 12/Day1 (n =110, 70) | 44.517 (± 8.212) | 44.357 (± 7.247) | | |
| Cycle 13/Day1 (n =92, 58) | 44.492 (± 7.972) | 45.261 (± 7.84) | | |
| Cycle 14/Day1 (n =81, 54) | 44.485 (± 8.204) | 44.898 (± 7.495) | | |
| Cycle 15/Day1 (n =61, 38) | 45.291 (± 7.095) | 45.053 (± 6.682) | | |
| Cycle 16/Day1 (n =52, 34) | 45.217 (± 7.656) | 44.445 (± 7.16) | | |
| Cycle 17/Day1 (n =47, 28) | 45.242 (± 7.344) | 44.438 (± 7.683) | | |
| Cycle 18/Day1 (n =36, 22) | 44.861 (± 7.769) | 44.182 (± 7.228) | | |
| Cycle 19/Day1 (n =29, 14) | 45.379 (± 6.662) | 45.026 (± 7.705) | | |
| Cycle 20/Day1 (n =20, 12) | 47.05 (± 5.375) | 44.78 (± 6.689) | | |
| Cycle 21/Day1 (n =15, 7) | 45.85 (± 5.209) | 44.494 (± 6.153) | | |
| End of treatment (n=163, 191) | 38.328 (± 9.472) | 38.457 (± 8.787) | | |
| Follow up (n =80, 110) | 41.919 (± 8.318) | 40.028 (± 9.048) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Functional Assessment of Cancer Therapy Kidney Symptom Index-Disease Related Symptoms (FKSI-DRS) Score

| End point title | Functional Assessment of Cancer Therapy Kidney Symptom Index-Disease Related Symptoms (FKSI-DRS) Score |
|---|---|

End point description:

FKSI-DRS was used to assess quality of life for those diagnosed with renal cell cancer and consisted of 9 items (lack of energy, pain, losing weight, bone pain, fatigue, short of breath, coughing, bothered by fevers, and hematuria). Each of the 9 items was answered on a 5-point Likert-type scale ranging from 0 to 4 (0= not at all, 1= a little bit, 2= somewhat, 3= quite a bit, 4= very much). Total FKSI-DRS score = sum of the 9 item scores; total range: 0 - 36; 0 (no symptoms) to 36 (very much); higher scores indicate greater presence of symptoms. FAS. Here, "n" signifies those subjects who were evaluable for the specified time points.

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

End point timeframe:

Baseline (Predose on Cycle 1 Day 1) , Day 1 of each cycle until Cycle 21, End of treatment (Day 670) and Follow-up visit (Day 698)

| **End point values** | Axitinib 5 mg | Sorafenib 400 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 361 | 362 | | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n =346, 341) | 28.874 (± 5.187) | 28.975 (± 5.193) | | |
| Cycle 2/Day1 (n =319, 295) | 28.211 (± 4.92) | 28.399 (± 5.064) | | |
| Cycle 3/Day1 (n =279, 244) | 28.64 (± 4.837) | 28.64 (± 4.868) | | |
| Cycle 4/Day1 (n =257, 220) | 28.822 (± 4.952) | 29.13 (± 4.322) | | |
| Cycle 5/Day1 (n =238, 202) | 28.869 (± 4.88) | 29.007 (± 4.379) | | |
| Cycle 6/Day1 (n =213, 178) | 29.159 (± 4.462) | 29.098 (± 4.697) | | |
| Cycle 7/Day1 (n =206, 157) | 29.042 (± 4.581) | 29.361 (± 4.558) | | |
| Cycle 8/Day1 (n =177, 135) | 29.52 (± 4.346) | 29.619 (± 4.386) | | |
| Cycle 9/Day1 (n =163, 117) | 29.194 (± 4.937) | 29.884 (± 3.838) | | |
| Cycle 10/Day1 (n =146, 96) | 29.343 (± 4.907) | 29.604 (± 3.959) | | |
| Cycle 11/Day1 (n =122, 85) | 29.762 (± 4.943) | 29.366 (± 4.404) | | |

| | | | | |
|---|---|---|---|---|
| Cycle 12/Day1 (n =110, 70) | 29.764 (± 4.507) | 29.257 (± 4.299) | | |
| Cycle 13/Day1 (n =92, 58) | 29.594 (± 4.205) | 29.666 (± 4.71) | | |
| Cycle 14/Day1 (n =81, 54) | 29.711 (± 4.313) | 29.82 (± 4.333) | | |
| Cycle 15/Day1 (n =61, 38) | 30.324 (± 3.582) | 29.5 (± 3.454) | | |
| Cycle 16/Day1 (n =52, 34) | 30.43 (± 3.443) | 29.474 (± 4.146) | | |
| Cycle 17/Day1 (n =47, 28) | 30.551 (± 3.331) | 28.737 (± 4.93) | | |
| Cycle 18/Day1 (n =36, 22) | 30.194 (± 3.992) | 29.045 (± 4.52) | | |
| Cycle 19/Day1 (n =29, 14) | 30.13 (± 3.636) | 29.286 (± 4.795) | | |
| Cycle 20/Day1 (n =20, 12) | 31.3 (± 2.736) | 29.25 (± 4.025) | | |
| Cycle 21/Day1 (n =15, 7) | 31.067 (± 3.173) | 30.143 (± 4.1) | | |
| End of Treatment (n =163, 191) | 26.288 (± 5.806) | 26.517 (± 5.614) | | |
| Follow up (n =80, 110) | 28.263 (± 4.802) | 27.516 (± 5.577) | | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Euro Quality of Life Questionnaire-5 Dimension (EQ-5D): Health State Profile Utility Score**

| End point title | Euro Quality of Life Questionnaire-5 Dimension (EQ-5D): Health State Profile Utility Score |
|---|---|

End point description:

EQ-5D: subject rated questionnaire to assess health-related quality of life in terms of a single utility or index score. Health state profile component assesses level of health for 5 domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each domain was rated on a 3-point response scale (1= no problems, 2= some/moderate problems and 3= extreme problems). Scoring formula developed by EuroQol Group assigned a utility value for each domain in the profile. Score were transformed and resulted in a total score range of 0 to 1, with higher scores indicating better health. FAS. Here, "n" signifies those subjects who were evaluable for the specified time points.

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

End point timeframe:

Baseline (Predose on Cycle 1 Day 1) , Day 1 of each cycle until Cycle 21, End of treatment (Day 670) and Follow-up visit (Day 698)

| **End point values** | Axitinib 5 mg | Sorafenib 400 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 361 | 362 | | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |

| | | | | |
|---|---|---|---|---|
| Baseline (n =347, 341) | 0.732 (± 0.275) | 0.731 (± 0.257) | | |
| Cycle 2/Day1 (n =326, 307) | 0.716 (± 0.267) | 0.696 (± 0.237) | | |
| Cycle 3/Day1 (n =287, 248) | 0.722 (± 0.243) | 0.709 (± 0.239) | | |
| Cycle 4/Day1 (n =262, 226) | 0.73 (± 0.236) | 0.716 (± 0.248) | | |
| Cycle 5/Day1 (n =244, 207) | 0.73 (± 0.237) | 0.711 (± 0.243) | | |
| Cycle 6/Day1 (n =221, 178) | 0.734 (± 0.23) | 0.704 (± 0.246) | | |
| Cycle 7/Day1 (n =213, 163) | 0.718 (± 0.267) | 0.728 (± 0.228) | | |
| Cycle 8/Day1 (n =181, 136) | 0.756 (± 0.236) | 0.702 (± 0.259) | | |
| Cycle 9/Day1 (n =169, 120) | 0.76 (± 0.227) | 0.73 (± 0.229) | | |
| Cycle 10/Day1 (n =151, 98) | 0.734 (± 0.243) | 0.73 (± 0.233) | | |
| Cycle 11/Day1 (n =126, 87) | 0.764 (± 0.235) | 0.724 (± 0.25) | | |
| Cycle 12/Day1 (n =110, 73) | 0.744 (± 0.244) | 0.734 (± 0.232) | | |
| Cycle 13/Day1 (n =96, 61) | 0.76 (± 0.211) | 0.753 (± 0.232) | | |
| Cycle 14/Day1 (n =80, 57) | 0.723 (± 0.239) | 0.752 (± 0.211) | | |
| Cycle 15/Day1 (n =63, 41) | 0.73 (± 0.255) | 0.758 (± 0.191) | | |
| Cycle 16/Day1 (n =54, 37) | 0.749 (± 0.22) | 0.785 (± 0.158) | | |
| Cycle 17/Day1 (n =48, 29) | 0.779 (± 0.186) | 0.764 (± 0.193) | | |
| Cycle 18/Day1 (n =37, 20) | 0.755 (± 0.204) | 0.755 (± 0.208) | | |
| Cycle 19/Day1 (n =29, 14) | 0.734 (± 0.253) | 0.804 (± 0.184) | | |
| Cycle 20/Day1 (n =21, 12) | 0.794 (± 0.22) | 0.771 (± 0.182) | | |
| Cycle 21/Day1 (n =16, 7) | 0.7 (± 0.273) | 0.771 (± 0.186) | | |
| End of Treatment (n =169, 196) | 0.608 (± 0.316) | 0.612 (± 0.31) | | |
| Follow up (n =76, 106) | 0.682 (± 0.294) | 0.666 (± 0.295) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Euro Quality of Life Questionnaire-5 Dimension (EQ-5D): Visual Analog Scale (VAS)

| End point title | Euro Quality of Life Questionnaire-5 Dimension (EQ-5D): Visual Analog Scale (VAS) |
|---|---|

End point description:

EQ-5D: subject rated questionnaire to assess health-related quality of life in terms of a single index value. VAS component: subjects rated their current health state on a scale from 0 (worst imaginable health state) to 100 (best imaginable health state); higher scores indicate a better health. FAS. Here,

"n" signifies those subjects who were evaluable for the specified time points.

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

End point timeframe:

Baseline (Predose on Cycle 1 Day 1) , Day 1 of each cycle until Cycle 21, End of treatment (Day 670) and Follow-up visit (Day 698)

| **End point values** | Axitinib 5 mg | Sorafenib 400 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 361 | 362 | | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n =341, 339) | 70.56 (± 19.187) | 70.351 (± 17.403) | | |
| Cycle 2/Day1 (n =317, 302) | 69.003 (± 20.195) | 67.606 (± 18.265) | | |
| Cycle 3/Day1 (n =280, 250) | 69.843 (± 17.927) | 69.712 (± 18.429) | | |
| Cycle 4/Day1 (n =261, 224) | 69.18 (± 18.636) | 70.759 (± 17.189) | | |
| Cycle 5/Day1 (n =244, 205) | 69.705 (± 18.33) | 71.888 (± 16.999) | | |
| Cycle 6/Day1 (n =220, 178) | 69.9 (± 18.168) | 71.365 (± 17.019) | | |
| Cycle 7/Day1 (n =209, 163) | 69.919 (± 18.063) | 72.282 (± 17.521) | | |
| Cycle 8/Day1 (n =180, 139) | 70.756 (± 19.183) | 71.475 (± 18.523) | | |
| Cycle 9/Day1 (n =168, 121) | 70.667 (± 18.556) | 73.38 (± 17.473) | | |
| Cycle 10/Day1 (n =151, 98) | 70.629 (± 18.68) | 75.102 (± 14.854) | | |
| Cycle 11/Day1 (n =126, 87) | 72.103 (± 18.064) | 74.586 (± 15.161) | | |
| Cycle 12/Day1 (n =111, 73) | 71.73 (± 17.276) | 73.959 (± 15.852) | | |
| Cycle 13/Day1 (n =94, 61) | 70.723 (± 19.147) | 75.693 (± 14.571) | | |
| Cycle 14/Day1 (n =81, 58) | 69.42 (± 20.286) | 75.362 (± 15.875) | | |
| Cycle 15/Day1 (n =62, 42) | 73.016 (± 15.325) | 75.357 (± 15.368) | | |
| Cycle 16/Day1 (n =52, 37) | 70.629 (± 19.272) | 73.676 (± 15.699) | | |
| Cycle 17/Day1 (n =48, 30) | 71.357 (± 17.84) | 73.676 (± 16.298) | | |
| Cycle 18/Day1 (n =37, 23) | 70.459 (± 18.853) | 73.87 (± 16.904) | | |
| Cycle 19/Day1 (n =29, 14) | 71.034 (± 16.963) | 70.571 (± 17.956) | | |
| Cycle 20/Day1 (n =21, 12) | 73.143 (± 15.347) | 66.917 (± 17.758) | | |
| Cycle 21/Day1 (n =16, 7) | 74.563 (± 16.054) | 64.714 (± 16.183) | | |
| End of Treatment (n =166, 197) | 61.759 (± 21.668) | 61.69 (± 20.973) | | |

| | | | | |
|---|---|---|---|---|
| Follow up (n =76, 109) | 64.382 (± 21.392) | 66.037 (± 19.754) | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From initiation of treatment up to follow-up period (up to 3 years)

Adverse event reporting additional description:

Same event may appear as both AE and SAE, what is presented are distinct event. Event may be classified as serious in 1 subject, nonserious in other, or 1 subject may have experienced both serious, nonserious event during study.

| | |
|---|---|
| Assessment type | Non-systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 18.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Axitinib 5 mg |

Reporting group description:

Axitinib (AG-013736) 5 mg tablet administered orally twice daily in cycles of 4 weeks.

| | |
|---|---|
| Reporting group title | Sorafenib 400 mg |

Reporting group description:

Sorafenib 400 mg tablet administered orally twice daily in cycles of 4 weeks.

| Serious adverse events | Axitinib 5 mg | Sorafenib 400 mg | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 146 / 359 (40.67%) | 127 / 355 (35.77%) | |
| number of deaths (all causes) | 55 | 42 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Metastasis | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastatic pain | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neoplasm progression | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal cell carcinoma | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tumour associated fever | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Accelerated hypertension | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 2 / 355 (0.56%) | |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertensive crisis | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypotension | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 359 (0.28%) | 4 / 355 (1.13%) | |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infarction | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jugular vein thrombosis | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subclavian vein thrombosis | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Surgical and medical procedures | | | |
| Pain management | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vertebroplasty | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| 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 | | | |
| Asthenia | | | |
| subjects affected / exposed | 2 / 359 (0.56%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Chest pain | | | |
| subjects affected / exposed | 2 / 359 (0.56%) | 2 / 355 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Chills | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Death | | | |
| subjects affected / exposed | 3 / 359 (0.84%) | 6 / 355 (1.69%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 6 | |
| deaths causally related to treatment / all | 3 / 3 | 4 / 6 | |
| Device dislocation | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Disease progression | | | |
| subjects affected / exposed | 32 / 359 (8.91%) | 18 / 355 (5.07%) | |
| occurrences causally related to treatment / all | 0 / 33 | 0 / 19 | |
| deaths causally related to treatment / all | 0 / 29 | 0 / 18 | |
| Fatigue | | | |
| subjects affected / exposed | 4 / 359 (1.11%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 3 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General physical health deterioration | | | |
| subjects affected / exposed | 3 / 359 (0.84%) | 5 / 355 (1.41%) | |
| occurrences causally related to treatment / all | 1 / 3 | 1 / 5 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 2 | |
| Hernia | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Impaired healing | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inflammation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malaise | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oedema | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain | | | |
| subjects affected / exposed | 2 / 359 (0.56%) | 3 / 355 (0.85%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 7 / 359 (1.95%) | 5 / 355 (1.41%) | |
| occurrences causally related to treatment / all | 3 / 8 | 6 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | Additional description: This event was gender specific. | | |
| subjects affected / exposed[1] | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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| Menometrorrhagia | Additional description: This event was gender specific. | | |
| subjects affected / exposed[2] | 0 / 96 (0.00%) | 1 / 104 (0.96%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vaginal polyp | Additional description: This event was gender specific. | | |
| subjects affected / exposed[3] | 1 / 96 (1.04%) | 0 / 104 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Respiratory, thoracic and mediastinal disorders** | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cough | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 7 / 359 (1.95%) | 3 / 355 (0.85%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemoptysis | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 2 / 355 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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| Haemothorax | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung disorder | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 3 / 359 (0.84%) | 5 / 355 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleurisy | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax | | | |
| subjects affected / exposed | 4 / 359 (1.11%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 1 / 4 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax spontaneous | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 7 / 359 (1.95%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 2 / 7 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Pulmonary haemorrhage | | | |

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| subjects affected / exposed | 0 / 359 (0.00%) | 2 / 355 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory distress | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Confusional state | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Disorientation | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mental status changes | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 4 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|---|---|---|---|
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 2 / 359 (0.56%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutrophil count abnormal | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 359 (0.28%) | 2 / 355 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femoral neck fracture | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal anastomotic leak | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Humerus fracture | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laceration | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lumbar vertebral fracture | | | |
| subjects affected / exposed | 2 / 359 (0.56%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Procedural pain | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radiation pneumonitis | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rib fracture | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Soft tissue injury | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal compression fracture | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 2 / 355 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 2 / 359 (0.56%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 2 / 355 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arrhythmia supraventricular | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arteriosclerosis coronary artery | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Atrial fibrillation | | | |

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|---|---|---|---|
| subjects affected / exposed | 2 / 359 (0.56%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial flutter | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrioventricular block | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bradycardia | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac arrest | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Cardiac failure | | | |
| subjects affected / exposed | 2 / 359 (0.56%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiopulmonary failure | | | |
| subjects affected / exposed | 2 / 359 (0.56%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 1 | |
| Congestive cardiomyopathy | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery insufficiency | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Haemorrhage coronary artery | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Mitral valve incompetence | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial infarction | | | |
| subjects affected / exposed | 6 / 359 (1.67%) | 4 / 355 (1.13%) | |
| occurrences causally related to treatment / all | 4 / 7 | 2 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prinzmetal angina | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Aphasia | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Balance disorder | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Central nervous system haemorrhage | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral infarction | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral ischaemia | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 2 / 359 (0.56%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Dizziness | | | |
| subjects affected / exposed | 3 / 359 (0.84%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Headache | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hemiparesis | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Leukoencephalopathy | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Loss of consciousness | | | |
| subjects affected / exposed | 2 / 359 (0.56%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningeal disorder | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Monoplegia | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Presyncope | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Seizure | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal cord compression | | | |

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|---|---|---|---|
| subjects affected / exposed | 2 / 359 (0.56%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| subjects affected / exposed | 2 / 359 (0.56%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 3 / 359 (0.84%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 3 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Blood and lymphatic system disorders** | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 8 / 355 (2.25%) | |
| occurrences causally related to treatment / all | 0 / 0 | 4 / 13 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Splenic infarction | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Eye disorders** | | | |
| Diplopia | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinal artery embolism | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinal artery occlusion | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinal vein occlusion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinal vein thrombosis | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 2 / 355 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal fistula | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ascites | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Constipation | | | |
| subjects affected / exposed | 2 / 359 (0.56%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 8 / 359 (2.23%) | 5 / 355 (1.41%) | |
| occurrences causally related to treatment / all | 6 / 8 | 3 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenal ulcer haemorrhage | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Enterocolitis | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric haemorrhage | | | |
| subjects affected / exposed | 2 / 359 (0.56%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric ulcer | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 5 / 355 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Gastrointestinal perforation | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inguinal hernia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 359 (0.84%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal obstruction | | | |
| subjects affected / exposed | 4 / 359 (1.11%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Melaena | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retroperitoneal haemorrhage | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Small intestinal obstruction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subileus | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 5 / 359 (1.39%) | 2 / 355 (0.56%) | |
| occurrences causally related to treatment / all | 2 / 5 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Biliary dilatation | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Budd-Chiari syndrome | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholangitis | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholelithiasis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic function abnormal | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Erythema multiforme | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 3 / 355 (0.85%) | |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Palmar-plantar erythrodysaesthesia syndrome | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pustular psoriasis | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rash | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 2 / 355 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urticaria | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |

| | | | |
|---|---|---|---|
| Acute kidney injury | | | |
| subjects affected / exposed | 4 / 359 (1.11%) | 2 / 355 (0.56%) | |
| occurrences causally related to treatment / all | 2 / 4 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute prerenal failure | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematuria | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephropathy | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Oliguria | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary retention | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypothyroidism | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Secondary hypothyroidism | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thyroiditis | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back pain | | | |
| subjects affected / exposed | 3 / 359 (0.84%) | 2 / 355 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Flank pain | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain in extremity | | | |
| subjects affected / exposed | 2 / 359 (0.56%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Polyarthritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal column stenosis | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spondylolisthesis | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Abdominal abscess | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 2 / 355 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aspergillus infection | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacterial diarrhoea | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Erysipelas | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infection | | | |
| subjects affected / exposed | 3 / 359 (0.84%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral discitis | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 4 / 355 (1.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection bacterial | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung infection | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscle abscess | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 5 / 359 (1.39%) | 4 / 355 (1.13%) | |
| occurrences causally related to treatment / all | 2 / 6 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia streptococcal | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia viral | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary tuberculosis | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 359 (0.28%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 2 / 355 (0.56%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 1 | |
| Septic shock | | | |
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 359 (0.56%) | 2 / 355 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 3 / 359 (0.84%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 3 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dehydration | | | |
| subjects affected / exposed | 10 / 359 (2.79%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 8 / 10 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 2 / 355 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 2 / 359 (0.56%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypocalcaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 359 (0.00%) | 1 / 355 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 2 / 359 (0.56%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 3 / 355 (0.85%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypovolaemia | | | |
| subjects affected / exposed | 1 / 359 (0.28%) | 0 / 355 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This event was gender specific.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This event was gender specific.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This event was gender specific.

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

| **Non-serious adverse events** | Axitinib 5 mg | Sorafenib 400 mg | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 336 / 359 (93.59%) | 334 / 355 (94.08%) | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 156 / 359 (43.45%) | 107 / 355 (30.14%) | |
| occurrences (all) | 318 | 174 | |
| Hypotension | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 19 / 359 (5.29%) | 6 / 355 (1.69%) | |
| occurrences (all) | 20 | 7 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 78 / 359 (21.73%) | 57 / 355 (16.06%) | |
| occurrences (all) | 203 | 120 | |
| Chest pain | | | |
| subjects affected / exposed | 23 / 359 (6.41%) | 20 / 355 (5.63%) | |
| occurrences (all) | 34 | 24 | |
| Fatigue | | | |
| subjects affected / exposed | 151 / 359 (42.06%) | 122 / 355 (34.37%) | |
| occurrences (all) | 366 | 210 | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 61 / 359 (16.99%) | 45 / 355 (12.68%) | |
| occurrences (all) | 99 | 83 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 22 / 359 (6.13%) | 22 / 355 (6.20%) | |
| occurrences (all) | 25 | 35 | |
| Pain | | | |
| subjects affected / exposed | 19 / 359 (5.29%) | 17 / 355 (4.79%) | |
| occurrences (all) | 23 | 19 | |
| Pyrexia | | | |
| subjects affected / exposed | 26 / 359 (7.24%) | 40 / 355 (11.27%) | |
| occurrences (all) | 31 | 59 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 68 / 359 (18.94%) | 70 / 355 (19.72%) | |
| occurrences (all) | 107 | 90 | |
| Dysphonia | | | |
| subjects affected / exposed | 116 / 359 (32.31%) | 49 / 355 (13.80%) | |
| occurrences (all) | 158 | 51 | |
| Dyspnoea | | | |
| subjects affected / exposed | 64 / 359 (17.83%) | 53 / 355 (14.93%) | |
| occurrences (all) | 100 | 78 | |
| Dyspnoea exertional | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 18 / 359 (5.01%) | 11 / 355 (3.10%) | |
| occurrences (all) | 21 | 13 | |
| Epistaxis | | | |
| subjects affected / exposed | 28 / 359 (7.80%) | 19 / 355 (5.35%) | |
| occurrences (all) | 37 | 20 | |
| Haemoptysis | | | |
| subjects affected / exposed | 8 / 359 (2.23%) | 18 / 355 (5.07%) | |
| occurrences (all) | 10 | 21 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 22 / 359 (6.13%) | 21 / 355 (5.92%) | |
| occurrences (all) | 37 | 28 | |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 33 / 359 (9.19%) | 21 / 355 (5.92%) | |
| occurrences (all) | 41 | 24 | |
| Investigations | | | |
| Blood thyroid stimulating hormone increased | | | |
| subjects affected / exposed | 19 / 359 (5.29%) | 11 / 355 (3.10%) | |
| occurrences (all) | 22 | 16 | |
| Lipase increased | | | |
| subjects affected / exposed | 13 / 359 (3.62%) | 22 / 355 (6.20%) | |
| occurrences (all) | 15 | 50 | |
| Weight decreased | | | |
| subjects affected / exposed | 111 / 359 (30.92%) | 83 / 355 (23.38%) | |
| occurrences (all) | 216 | 168 | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 33 / 359 (9.19%) | 21 / 355 (5.92%) | |
| occurrences (all) | 42 | 28 | |
| Dysgeusia | | | |
| subjects affected / exposed | 43 / 359 (11.98%) | 31 / 355 (8.73%) | |
| occurrences (all) | 56 | 32 | |
| Headache | | | |
| subjects affected / exposed | 55 / 359 (15.32%) | 43 / 355 (12.11%) | |
| occurrences (all) | 78 | 59 | |
| Blood and lymphatic system disorders | | | |

| | | | |
|---|---|---|---|
| Anaemia | | | |
| subjects affected / exposed | 18 / 359 (5.01%) | 44 / 355 (12.39%) | |
| occurrences (all) | 28 | 106 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 55 / 359 (15.32%) | 46 / 355 (12.96%) | |
| occurrences (all) | 95 | 69 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 37 / 359 (10.31%) | 16 / 355 (4.51%) | |
| occurrences (all) | 50 | 20 | |
| Constipation | | | |
| subjects affected / exposed | 79 / 359 (22.01%) | 82 / 355 (23.10%) | |
| occurrences (all) | 116 | 101 | |
| Diarrhoea | | | |
| subjects affected / exposed | 208 / 359 (57.94%) | 195 / 355 (54.93%) | |
| occurrences (all) | 736 | 449 | |
| Dyspepsia | | | |
| subjects affected / exposed | 39 / 359 (10.86%) | 15 / 355 (4.23%) | |
| occurrences (all) | 46 | 22 | |
| Flatulence | | | |
| subjects affected / exposed | 20 / 359 (5.57%) | 8 / 355 (2.25%) | |
| occurrences (all) | 22 | 10 | |
| Nausea | | | |
| subjects affected / exposed | 128 / 359 (35.65%) | 84 / 355 (23.66%) | |
| occurrences (all) | 212 | 138 | |
| Stomatitis | | | |
| subjects affected / exposed | 60 / 359 (16.71%) | 47 / 355 (13.24%) | |
| occurrences (all) | 113 | 87 | |
| Vomiting | | | |
| subjects affected / exposed | 95 / 359 (26.46%) | 69 / 355 (19.44%) | |
| occurrences (all) | 161 | 100 | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 18 / 359 (5.01%) | 122 / 355 (34.37%) | |
| occurrences (all) | 20 | 145 | |
| Dry skin | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 36 / 359 (10.03%) | 42 / 355 (11.83%) | |
| occurrences (all) | 47 | 47 | |
| Erythema | | | |
| subjects affected / exposed | 12 / 359 (3.34%) | 39 / 355 (10.99%) | |
| occurrences (all) | 14 | 52 | |
| Palmar-plantar erythrodysaesthesia syndrome | | | |
| subjects affected / exposed | 100 / 359 (27.86%) | 183 / 355 (51.55%) | |
| occurrences (all) | 339 | 484 | |
| Pruritus | | | |
| subjects affected / exposed | 25 / 359 (6.96%) | 48 / 355 (13.52%) | |
| occurrences (all) | 30 | 59 | |
| Rash | | | |
| subjects affected / exposed | 53 / 359 (14.76%) | 109 / 355 (30.70%) | |
| occurrences (all) | 72 | 168 | |
| Renal and urinary disorders | | | |
| Proteinuria | | | |
| subjects affected / exposed | 49 / 359 (13.65%) | 32 / 355 (9.01%) | |
| occurrences (all) | 219 | 72 | |
| Endocrine disorders | | | |
| Hypothyroidism | | | |
| subjects affected / exposed | 74 / 359 (20.61%) | 33 / 355 (9.30%) | |
| occurrences (all) | 89 | 36 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 62 / 359 (17.27%) | 46 / 355 (12.96%) | |
| occurrences (all) | 111 | 55 | |
| Back pain | | | |
| subjects affected / exposed | 59 / 359 (16.43%) | 54 / 355 (15.21%) | |
| occurrences (all) | 96 | 65 | |
| Muscle spasms | | | |
| subjects affected / exposed | 11 / 359 (3.06%) | 21 / 355 (5.92%) | |
| occurrences (all) | 14 | 30 | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 28 / 359 (7.80%) | 27 / 355 (7.61%) | |
| occurrences (all) | 41 | 31 | |
| Myalgia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 28 / 359 (7.80%) | 12 / 355 (3.38%) | |
| occurrences (all) | 43 | 15 | |
| Pain in extremity | | | |
| subjects affected / exposed | 49 / 359 (13.65%) | 53 / 355 (14.93%) | |
| occurrences (all) | 82 | 87 | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 25 / 359 (6.96%) | 13 / 355 (3.66%) | |
| occurrences (all) | 33 | 13 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 140 / 359 (39.00%) | 112 / 355 (31.55%) | |
| occurrences (all) | 279 | 161 | |
| Dehydration | | | |
| subjects affected / exposed | 18 / 359 (5.01%) | 10 / 355 (2.82%) | |
| occurrences (all) | 26 | 10 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported