Clinical trial results:
AG-013736 (Axitinib) for the Treatment of Metastatic Renal Cell Cancer

Summary

EudraCT number	2010-018585-23
Trial protocol	BG
Global end of trial date	29 April 2021

Results information

Result version number	v1 (current)
This version publication date	06 May 2022
First version publication date	06 May 2022

Trial information

Trial identification

Sponsor protocol code	A4061051

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00920816
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 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 18007181021, 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 July 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 April 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Compare the progression-free survival (PFS) of treatment-naïve subjects with metastatic renal cell carcinoma (mRCC) receiving AG-013736 versus sorafenib.

Estimate the PFS of previously-treated Asian subjects with mRCC receiving AG-013736 versus sorafenib.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 August 2009
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bosnia and Herzegovina: 11
Country: Number of subjects enrolled	Bulgaria: 2
Country: Number of subjects enrolled	Chile: 29
Country: Number of subjects enrolled	India: 35
Country: Number of subjects enrolled	Malaysia: 6
Country: Number of subjects enrolled	Mexico: 11
Country: Number of subjects enrolled	Philippines: 14
Country: Number of subjects enrolled	Romania: 14
Country: Number of subjects enrolled	Russian Federation: 58
Country: Number of subjects enrolled	South Africa: 1
Country: Number of subjects enrolled	Ukraine: 61
Country: Number of subjects enrolled	United States: 29
Country: Number of subjects enrolled	Taiwan: 6
Worldwide total number of subjects	277
EEA total number of subjects	16

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)	213
From 65 to 84 years	63
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

First-line subjects included all treatment-naive subjects with metastatic renal cell cancer (mRCC) from global and second-line subjects included all previously-treated Asian subjects with mRCC.

Pre-assignment

Screening details:

All China subjects were excluded from safety analysis due to inability to obtain timely approval to use data in accordance with Human Genetic Resources Administration of China (HGRAC) regulation.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Axitinib (First-line Subjects)

Arm description:

Subjects (excluding subjects from China) with no prior systemic first-line therapy received axitinib (AG-013736) tablet at a starting dose of 5 milligram (mg) orally twice daily, dose adjustment was done based on the tolerability, as per investigator's discretion. Study medication was administered in cycles of 4 weeks.

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

Dosage and administration details:

5 mg

Arm title	Sorafenib (First-line Subjects)

Arm description:

Subjects (excluding subjects from China) with no prior systemic first-line therapy received sorafenib tablet at a starting dose of 400 mg orally twice daily, dose adjustment was done based on the tolerability, as per investigator's discretion. Study medication was administered in cycles of 4 weeks.

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

Dosage and administration details:

400 mg

Arm title	Axitinib (Second-line Subjects)

Arm description:

Asian subjects (excluding subjects from China) with prior systemic first-line therapy containing sunitinib or cytokine received axitinib (AG-013736) tablet at a starting dose of 5 mg orally twice daily, dose adjustment was done based on the tolerability, as per investigator's discretion. Study medication was administered in cycles of 4 weeks.

Arm type	Experimental

Investigational medicinal product name	Axitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

5 mg

Arm title	Sorafenib (Second-line Subjects)

Arm description:

Asian subjects (excluding subjects from China) with prior systemic first-line therapy containing sunitinib or cytokine received sorafenib tablet at a starting dose of 400 mg orally twice daily, dose adjustment was done based on the tolerability, as per investigator's discretion. Study medication was administered in cycles of 4 weeks.

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

Dosage and administration details:

5 mg

Number of subjects in period 1	Axitinib (First-line Subjects)	Sorafenib (First-line Subjects)	Axitinib (Second-line Subjects)
Started	173	88	11
Completed	0	0	0
Not completed	173	88	11
Global deterioration of health status	2	-	-
Subject refused treatment	11	5	1
Adverse event	1	1	1
Subject died	116	63	8
Unspecified	26	15	1
Objective progression or relapse	6	2	-
Lost to follow-up	11	2	-

Number of subjects in period 1	Sorafenib (Second-line Subjects)
Started	5
Completed	0
Not completed	5
Global deterioration of health status	-
Subject refused treatment	-
Adverse event	-
Subject died	3
Unspecified	2
Objective progression or relapse	-

Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	Axitinib (First-line Subjects)
Reporting group description:	
Subjects (excluding subjects from China) with no prior systemic first-line therapy received axitinib (AG-013736) tablet at a starting dose of 5 milligram (mg) orally twice daily, dose adjustment was done based on the tolerability, as per investigator's discretion. Study medication was administered in cycles of 4 weeks.	
Reporting group title	Sorafenib (First-line Subjects)
Reporting group description:	
Subjects (excluding subjects from China) with no prior systemic first-line therapy received sorafenib tablet at a starting dose of 400 mg orally twice daily, dose adjustment was done based on the tolerability, as per investigator's discretion. Study medication was administered in cycles of 4 weeks.	
Reporting group title	Axitinib (Second-line Subjects)
Reporting group description:	
Asian subjects (excluding subjects from China) with prior systemic first-line therapy containing sunitinib or cytokine received axitinib (AG-013736) tablet at a starting dose of 5 mg orally twice daily, dose adjustment was done based on the tolerability, as per investigator's discretion. Study medication was administered in cycles of 4 weeks.	
Reporting group title	Sorafenib (Second-line Subjects)
Reporting group description:	
Asian subjects (excluding subjects from China) with prior systemic first-line therapy containing sunitinib or cytokine received sorafenib tablet at a starting dose of 400 mg orally twice daily, dose adjustment was done based on the tolerability, as per investigator's discretion. Study medication was administered in cycles of 4 weeks.	

Reporting group values	Axitinib (First-line Subjects)	Sorafenib (First-line Subjects)	Axitinib (Second-line Subjects)
Number of subjects	173	88	11
Age Categorical Units: Subjects			
18-64 years	126	72	10
>=65 years	47	16	1
Sex: Female, Male Units: Subjects			
Male	122	69	8
Female	51	19	3

Reporting group values	Sorafenib (Second-line Subjects)	Total	
Number of subjects	5	277	
Age Categorical Units: Subjects			
18-64 years	5	213	
>=65 years	0	64	
Sex: Female, Male Units: Subjects			
Male	3	202	
Female	2	75	

End points

End points reporting groups

Reporting group title	Axitinib (First-line Subjects)

Reporting group description:

Subjects (excluding subjects from China) with no prior systemic first-line therapy received axitinib (AG-013736) tablet at a starting dose of 5 milligram (mg) orally twice daily, dose adjustment was done based on the tolerability, as per investigator’s discretion. Study medication was administered in cycles of 4 weeks.

Reporting group title	Sorafenib (First-line Subjects)

Reporting group description:

Subjects (excluding subjects from China) with no prior systemic first-line therapy received sorafenib tablet at a starting dose of 400 mg orally twice daily, dose adjustment was done based on the tolerability, as per investigator’s discretion. Study medication was administered in cycles of 4 weeks.

Reporting group title	Axitinib (Second-line Subjects)

Reporting group description:

Asian subjects (excluding subjects from China) with prior systemic first-line therapy containing sunitinib or cytokine received axitinib (AG-013736) tablet at a starting dose of 5 mg orally twice daily, dose adjustment was done based on the tolerability, as per investigator’s discretion. Study medication was administered in cycles of 4 weeks.

Reporting group title	Sorafenib (Second-line Subjects)

Reporting group description:

Asian subjects (excluding subjects from China) with prior systemic first-line therapy containing sunitinib or cytokine received sorafenib tablet at a starting dose of 400 mg orally twice daily, dose adjustment was done based on the tolerability, as per investigator’s discretion. Study medication was administered in cycles of 4 weeks.

Subject analysis set title	Axitinib (First-line Subjects): PCD
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects with no prior systemic first-line therapy received axitinib (AG-013736) tablet at a starting dose of 5 milligram (mg) orally twice daily, dose adjustment was done based on the tolerability, as per investigator's discretion. Study medication was administered in cycles of 4 weeks.

Subject analysis set title	Sorafenib (First-line Subjects): PCD
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects with no prior systemic first-line therapy received sorafenib tablet at a starting dose of 400 mg orally twice daily, dose adjustment was done based on the tolerability, as per investigator's discretion. Study medication was administered in cycles of 4 weeks.

Subject analysis set title	Axitinib (Second-line Subjects): PCD
Subject analysis set type	Full analysis

Subject analysis set description:

All Asian subjects with prior systemic first-line therapy containing sunitinib or cytokine received axitinib (AG-013736) tablet at a starting dose of 5 mg orally twice daily, dose adjustment was done based on the tolerability, as per investigator's discretion. Study medication was administered in cycles of 4 weeks.

Subject analysis set title	Sorafenib (Second-line Subjects): PCD
Subject analysis set type	Full analysis

Subject analysis set description:

All Asian subjects with prior systemic first-line therapy containing sunitinib or cytokine received sorafenib tablet at a starting dose of 400 mg orally twice daily, dose adjustment was done based on the tolerability, as per investigator's discretion. Study medication was administered in cycles of 4 weeks.

Primary: Progression Free Survival (PFS): First-Line Subjects

End point title	Progression Free Survival (PFS): First-Line Subjects

End point description:

Time in months from randomisation to first documentation of objective tumour progression or death due to any cause. PFS calculated as (first event date minus date of randomisation plus 1)/30.4. Tumour

progression determined from oncologic assessment data (where it meets criteria for progressive disease [PD]), or from adverse event (AE) data (where outcome was "Death"). Progression using Response Evaluation Criteria in Solid Tumours (RECIST) is >= 20 percent (%) increase in sum of longest diameter of target lesions; measurable increase in non-target lesion; appearance of new lesions. Full analysis set (FAS) included all previously-treated Asian subjects who were randomised, with study drug assignment designated according to initial randomisation, regardless of whether subjects received study drug, or received a different drug from that to which they were randomised.

End point type	Primary

End point timeframe:

Baseline until disease progression or death (assessed on Week 6, Week 12 and thereafter every 8 weeks up to Week 107)

End point values	Axitinib (First-line Subjects): PCD	Sorafenib (First-line Subjects): PCD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	192	96		
Units: months				
median (confidence interval 95%)	10.1 (7.2 to 12.1)	6.5 (4.7 to 8.3)		

Statistical analyses

Statistical analysis title	Axitinib vs Sorafenib: First line, PCD

Statistical analysis description:

First-line subjects: hazard ratio was stratified by eastern cooperative oncology group (ECOG) performance status (0 versus 1).

Comparison groups	Axitinib (First-line Subjects): PCD v Sorafenib (First-line Subjects): PCD
Number of subjects included in analysis	288
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.767
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.559
upper limit	1.053

Primary: Progression Free Survival (PFS): Second-Line Subjects

End point title	Progression Free Survival (PFS): Second-Line Subjects

End point description:

Time in months from randomisation to first documentation of objective tumour progression or death due to any cause. PFS calculated as (first event date minus date of randomisation plus 1)/30.4. Tumour progression determined from oncologic assessment data (where it meets criteria for progressive disease [PD]), or from adverse event (AE) data (where outcome was "Death"). Progression using Response Evaluation Criteria in Solid Tumours (RECIST) is >= 20% increase in sum of longest diameter of target lesions; measurable increase in non-target lesion; appearance of new lesions. FAS included all

previously-treated Asian subjects who were randomised, with study drug assignment designated according to initial randomisation, regardless of whether subjects received study drug, or received a different drug from that to which they were randomised.

End point type	Primary

End point timeframe:

Baseline until disease progression or death (assessed on Week 6, Week 12 and thereafter every 8 weeks up to Week 103)

End point values	Axitinib (Second-line Subjects): PCD	Sorafenib (Second-line Subjects): PCD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	135	69		
Units: months				
median (confidence interval 95%)	6.5 (4.7 to 9.1)	4.8 (3.0 to 6.5)		

Statistical analyses

Statistical analysis title	Axitinib vs Sorafenib: Second line, PCD

Statistical analysis description:

Second-line subjects: hazard ratio was stratified by eastern cooperative oncology group (ECOG) performance status (0 versus 1) and prior treatment (sunitinib versus cytokine-containing regimen).

Comparison groups	Axitinib (Second-line Subjects): PCD v Sorafenib (Second-line Subjects): PCD
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.731
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.506
upper limit	1.058

Secondary: Percentage of Subjects With Objective Response (OR): First-Line Subjects

End point title	Percentage of Subjects With Objective Response (OR): First-Line Subjects

End point description:

Percentage of subjects with OR based on assessment of confirmed complete response (CR) or confirmed partial response (PR) according to RECIST. Confirmed response were those that persisted on repeat imaging study at least 4 weeks after initial documentation of response. CR was defined as disappearance of all lesions (target and/or non target). PR were those with at least 30% decrease in sum of the longest dimensions of target lesions taking as a reference the baseline sum longest dimensions, with non target lesions not increased or absent. FAS included all previously-treated Asian subjects who were randomised, with study drug assignment designated according to initial randomisation, regardless of whether subjects received study drug, or received a different drug from that to which they were randomised.

End point type	Secondary

End point timeframe:

Baseline until disease progression or death (assessed on Week 6, Week 12 and thereafter every 8 weeks up to Week 107)

End point values	Axitinib (First-line Subjects): PCD	Sorafenib (First-line Subjects): PCD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	192	96		
Units: percentage of subjects				
number (confidence interval 95%)	32.3 (25.7 to 39.4)	14.6 (8.2 to 23.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Objective Response (OR): Second-Line Subjects

End point title	Percentage of Subjects With Objective Response (OR): Second-Line Subjects

End point description:

Percentage of subjects with OR based on assessment of confirmed complete response (CR) or confirmed partial response (PR) according to RECIST. Confirmed response were those that persisted on repeat imaging study at least 4 weeks after initial documentation of response. CR was defined as disappearance of all lesions (target and/or non target). PR were those with at least 30% decrease in sum of the longest dimensions of target lesions taking as a reference the baseline sum longest dimensions, with non target lesions not increased or absent. FAS included all previously-treated Asian subjects who were randomised, with study drug assignment designated according to initial randomisation, regardless of whether subjects received study drug, or received a different drug from that to which they were randomised.

End point type	Secondary

End point timeframe:

Baseline until disease progression or death (assessed on Week 6, Week 12 and thereafter every 8 weeks up to Week 103)

End point values	Axitinib (Second-line Subjects): PCD	Sorafenib (Second-line Subjects): PCD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	135	69		
Units: percentage of subjects				
number (confidence interval 95%)	23.7 (16.8 to 31.8)	10.1 (4.2 to 19.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DR): First-Line Subjects

End point title	Duration of Response (DR): First-Line Subjects

End point description:

Time in months from the first documentation of objective tumour response that is subsequently confirmed to objective tumour progression or death due to any cause. Duration of tumour response was calculated as (the date of the first documentation of objective tumour progression or death due to any cause minus the date of the first CR or PR that was subsequently confirmed plus 1) divided by 30.4. DR was calculated for the subgroup of subjects with a confirmed objective tumour response. DR was calculated for the subgroup of subjects from the FAS treatment-naive population, with a confirmed objective tumour response (CR or PR). '99999' signifies that upper limit of CI was not estimable because subjects were still responding to medication as the study was ongoing at the time of primary completion analysis and this analysis was final.

End point type	Secondary

End point timeframe:

Baseline until disease progression or death (assessed on Week 6, Week 12 and thereafter every 8 weeks up to Week 107)

End point values	Axitinib (First-line Subjects): PCD	Sorafenib (First-line Subjects): PCD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	62	14		
Units: months				
median (confidence interval 95%)	14.7 (11.0 to 99999)	14.3 (11.3 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DR): Second-Line Subjects

End point title	Duration of Response (DR): Second-Line Subjects

End point description:

Time in months from the first documentation of objective tumour response that is subsequently confirmed to objective tumour progression or death due to any cause. Duration of tumour response was calculated as (the date of the first documentation of objective tumour progression or death due to any cause minus the date of the first CR or PR that was subsequently confirmed plus 1) divided by 30.4. DR was calculated for the subgroup of subjects with a confirmed objective tumour response. DR was calculated for the subgroup of subjects from the FAS previously-treated population, with a confirmed objective tumour response (CR or PR). '99999' signifies that median and upper limit of CI was not estimable because subjects were still responding to medication as the study was ongoing at the time of primary completion analysis and this analysis was final.

End point type	Secondary

End point timeframe:

Baseline until disease progression or death (assessed on Week 6, Week 12 and thereafter every 8 weeks up to Week 103)

End point values	Axitinib (Second-line Subjects): PCD	Sorafenib (Second-line Subjects): PCD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	7		
Units: months				
median (confidence interval 95%)	99999 (12.5 to 99999)	8.7 (4.1 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS): First-Line Subjects

End point title	Overall Survival (OS): First-Line Subjects

End point description:

Time in months from date of randomisation to date of death due to any cause. OS was calculated as (the death date minus the date of randomisation plus 1) divided by 30.4. Death was determined from adverse event data (where outcome was death) or from follow-up contact data (where the subject current status was death). FAS included all treatment-naive subjects who were randomised, with study drug assignment designated according to initial randomisation, regardless of whether subjects received study drug, or received a different drug from that to which they were randomised. "99999" signifies that median and upper limit of the CI was not reachable as data was not matured at the time of the analysis as the study was ongoing at the time of primary completion analysis and this analysis was final.

End point type	Secondary

End point timeframe:

Baseline until death (assessed on Week 6, Week 12 and thereafter every 8 weeks up to Week 107)

End point values	Axitinib (First-line Subjects): PCD	Sorafenib (First-line Subjects): PCD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	192	96		
Units: months				
median (confidence interval 95%)	99999 (18.1 to 99999)	99999 (18.1 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS): Second-Line Subjects

End point title	Overall Survival (OS): Second-Line Subjects

End point description:

Time in months from date of randomisation to date of death due to any cause. OS was calculated as (the death date minus the date of randomisation plus 1) divided by 30.4. Death was determined from adverse event data (where outcome was death) or from follow-up contact data (where the subject current status was death). FAS included all treatment-naive subjects who were randomised, with study drug assignment designated according to initial randomisation, regardless of whether subjects received study drug, or received a different drug from that to which they were randomised. "99999" signifies that upper limit of the CI was not reachable as data was not matured at the time of the analysis as the study was ongoing at the time of primary completion analysis and this analysis was final.

End point type	Secondary

End point timeframe:

Baseline until death (assessed on Week 6, Week 12 and thereafter every 8 weeks up to Week 103)

End point values	Axitinib (Second-line Subjects): PCD	Sorafenib (Second-line Subjects): PCD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	135	69		
Units: months				
median (confidence interval 95%)	17.2 (14.8 to 99999)	18.1 (12.1 to 99999)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Functional Assessment of Cancer Therapy Kidney Symptom Index-15 (FKSI-15): First-Line Subjects

End point title	Functional Assessment of Cancer Therapy Kidney Symptom Index-15 (FKSI-15): First-Line Subjects

End point description:

FKSI-15 questionnaires (lack of energy, side effects, pain, weight loss, bone pain, fatigue, enjoying life, short of breath, worsened condition, appetite, coughing, bothered by fevers, ability to work, hematuria, sleep) was used to assess quality of life (QoL) for those diagnosed with renal cell cancer. Questions answered on 5-point Likert scale: 0 to 4 (0= not at all, 1= little bit, 2= somewhat, 3= quite a bit, 4= very much). Total FKSI score 0 to 60; higher scores=better health states (Individual questions may be reversed coded, as appropriate). FAS treatment-naive population. Here 'Number of subjects analysed' signifies those subjects who were evaluable for this endpoint and 'n' signifies those subjects evaluated for this endpoint at specific time points for each group respectively.

End point type	Other pre-specified

End point timeframe:

Baseline (Pre-dose on Cycle [C]1 Day [D]1), D1 of each cycle until C23, end of treatment (up to Week 107), follow-up (28 days after last dose)

End point values	Axitinib (First-line Subjects): PCD	Sorafenib (First-line Subjects): PCD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	183	95		
Units: units on a scale				
arithmetic mean (standard deviation)				
C1 D1 (n= 183, 95)	43.869 (± 8.117)	43.865 (± 6.723)		
C2 D1 (n= 176, 90)	43.328 (± 7.630)	43.969 (± 6.286)		
C3 D1 (n= 164, 84)	43.366 (± 7.192)	43.345 (± 6.878)		
C4 D1 (n= 156, 81)	42.932 (± 7.566)	42.926 (± 7.324)		
C5 D1 (n= 153, 77)	43.211 (± 7.578)	44.022 (± 6.714)		
C6 D1 (n= 141, 72)	42.787 (± 8.098)	42.344 (± 6.685)		
C7 D1 (n= 139, 65)	42.474 (± 7.926)	43.446 (± 6.931)		
C8 D1 (n= 131, 60)	42.534 (± 7.510)	44.077 (± 6.986)		
C9 D1 (n= 126, 59)	42.778 (± 8.229)	44.051 (± 7.234)		
C10 D1 (n= 122, 55)	43.120 (± 7.966)	44.018 (± 6.751)		
C11 D1 (n= 114, 48)	43.264 (± 7.837)	45.000 (± 6.130)		
C12 D1 (n= 105, 44)	43.962 (± 7.243)	45.318 (± 6.440)		
C13 D1 (n= 99, 44)	44.141 (± 7.289)	45.787 (± 6.526)		
C14 D1 (n= 95, 37)	43.789 (± 7.985)	45.459 (± 6.535)		
C15 D1 (n= 85, 37)	44.176 (± 8.055)	45.514 (± 5.914)		
C16 D1 (n= 82, 33)	44.232 (± 7.515)	46.000 (± 5.651)		
C17 D1 (n= 78, 30)	43.897 (± 8.456)	46.400 (± 6.262)		
C18 D1 (n= 71, 28)	43.761 (± 8.019)	45.357 (± 6.983)		
C19 D1 (n= 57, 24)	43.737 (± 7.413)	45.583 (± 7.366)		
C20 D1 (n= 45, 21)	43.733 (± 7.605)	44.333 (± 7.066)		
C21 D1 (n= 36, 18)	45.417 (± 6.240)	43.500 (± 7.687)		
C22 D1 (n= 23, 12)	47.000 (± 5.985)	45.833 (± 5.937)		
C23 D1 (n= 14, 7)	47.571 (± 6.357)	45.714 (± 6.651)		
End of treatment (n= 72, 42)	39.052 (± 9.109)	39.524 (± 8.896)		
Follow-up (n= 41, 26)	39.683 (± 11.132)	40.038 (± 9.897)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Functional Assessment of Cancer Therapy Kidney Symptom Index-15 (FKSI-15): Second-Line Subjects

End point title	Functional Assessment of Cancer Therapy Kidney Symptom Index-15 (FKSI-15): Second-Line Subjects

End point description:

FKSI-15 questionnaires (lack of energy, side effects, pain, weight loss, bone pain, fatigue, enjoying life, short of breath, worsened condition, appetite, coughing, bothered by fevers, ability to work, hematuria, sleep) was used to assess quality of life (QoL) for those diagnosed with renal cell cancer. Questions answered on 5-point Likert scale: 0 to 4 (0= not at all, 1= little bit, 2= somewhat, 3= quite a bit, 4= very much). Total FKSI score 0 to 60; higher scores=better health states (Individual questions may be reversed coded, as appropriate). FAS previously-treated Asian population. Here 'Number of subjects analysed' signifies those subjects who were evaluable for this endpoint and 'n' signifies those subjects evaluated for this endpoint at specific time points for each group respectively.

End point type	Other pre-specified

End point timeframe:

Baseline (Pre-dose on Cycle [C]1 Day [D]1), D1 of each cycle until C21, end of treatment (up to Week 103), follow-up (28 days after last dose)

End point values	Axitinib (Second-line Subjects): PCD	Sorafenib (Second-line Subjects): PCD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	134	69		
Units: units on a scale				
arithmetic mean (standard deviation)				
C1 D1 (n= 134, 69)	46.753 (± 6.692)	47.470 (± 7.450)		
C2 D1 (n= 127, 66)	46.217 (± 7.028)	45.045 (± 7.478)		
C3 D1 (n= 124, 57)	45.968 (± 7.237)	45.684 (± 7.756)		
C4 D1 (n= 116, 53)	45.060 (± 8.040)	45.792 (± 7.762)		
C5 D1 (n= 111, 48)	45.775 (± 7.797)	46.125 (± 7.491)		
C6 D1 (n= 108, 41)	45.407 (± 7.274)	46.341 (± 7.213)		
C7 D1 (n= 100, 38)	45.709 (± 8.263)	45.053 (± 7.843)		
C8 D1 (n= 89, 37)	45.169 (± 7.609)	45.676 (± 9.357)		
C9 D1 (n= 82, 33)	45.829 (± 7.442)	45.970 (± 8.487)		
C10 D1 (n= 74, 27)	45.608 (± 8.299)	46.148 (± 8.156)		
C11 D1 (n= 66, 22)	45.833 (± 7.599)	47.227 (± 6.611)		
C12 D1 (n= 59, 22)	45.797 (± 6.967)	48.091 (± 6.414)		
C13 D1 (n= 55, 20)	46.727 (± 7.307)	47.600 (± 5.762)		
C14 D1 (n= 50, 15)	47.740 (± 7.094)	49.133 (± 5.235)		

C15 D1 (n= 44, 13)	48.023 (± 6.297)	49.308 (± 4.111)		
C16 D1 (n= 38, 12)	48.184 (± 6.186)	50.500 (± 3.989)		
C17 D1 (n= 33, 10)	47.909 (± 6.866)	49.000 (± 5.869)		
C18 D1 (n= 29, 8)	48.138 (± 6.791)	49.125 (± 5.139)		
C19 D1 (n= 22, 7)	48.636 (± 5.206)	48.571 (± 7.458)		
C20 D1 (n= 21, 6)	48.810 (± 6.478)	50.500 (± 4.637)		
C21 D1 (n= 16, 6)	50.188 (± 5.588)	50.000 (± 5.177)		
End of treatment (n= 37, 27)	41.432 (± 9.188)	42.889 (± 8.846)		
Follow-up (n= 13, 12)	35.385 (± 7.795)	38.583 (± 11.556)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Functional Assessment of Cancer Therapy Kidney Symptom Index -Disease Related Symptoms (FKSI-DRS): First-Line Subjects

End point title	Functional Assessment of Cancer Therapy Kidney Symptom Index -Disease Related Symptoms (FKSI-DRS): First-Line Subjects

End point description:

FKSI-DRS: subset of FKSI which is FACT–Kidney Symptom Index questionnaire used to assess QoL for subjects diagnosed with renal cell cancer. FKSI contains 15 questions and FKSI-DRS 9 questions (lack of energy, pain, losing weight, bone pain, fatigue, short of breath, coughing, bothered by fevers, hematuria) each ranging from 0 (not at all) to 4 (very much). FKSI-DRS total score 0 to 36; higher scores associated with better health states (Individual questions may be reversed coded, as appropriate). FAS treatment-naive population. Here 'Number of subjects analysed' signifies those subjects who were evaluable for this endpoint and 'n' signifies those subjects evaluated for this endpoint at specific time points for each group respectively.

End point type	Other pre-specified

End point timeframe:

Baseline (Pre-dose on Cycle [C]1 Day [D]1), D1 of each cycle until C23, end of treatment (up to Week 107), follow-up (28 days after last dose)

End point values	Axitinib (First-line Subjects): PCD	Sorafenib (First-line Subjects): PCD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	183	95		
Units: units on a scale				
arithmetic mean (standard deviation)				
C1 D1 (n= 183, 95)	28.691 (± 5.392)	29.653 (± 4.699)		
C2 D1 (n= 176, 90)	28.728 (± 4.581)	29.963 (± 3.817)		

C3 D1 (n= 164, 84)	29.171 (± 4.093)	29.750 (± 4.095)		
C4 D1 (n= 156, 81)	28.577 (± 4.305)	29.642 (± 4.244)		
C5 D1 (n= 153, 77)	29.020 (± 4.257)	30.255 (± 3.668)		
C6 D1 (n= 141, 72)	28.574 (± 4.674)	29.153 (± 4.009)		
C7 D1 (n= 139, 65)	28.568 (± 4.548)	29.523 (± 4.051)		
C8 D1 (n= 131, 60)	28.557 (± 4.308)	30.296 (± 3.890)		
C9 D1 (n= 126, 59)	28.817 (± 4.665)	30.186 (± 4.392)		
C10 D1 (n= 122, 55)	29.057 (± 4.484)	30.364 (± 4.143)		
C11 D1 (n= 114, 48)	29.146 (± 4.207)	30.688 (± 3.926)		
C12 D1 (n= 105, 44)	29.648 (± 3.752)	30.727 (± 3.896)		
C13 D1 (n= 99, 44)	29.545 (± 4.056)	31.483 (± 3.602)		
C14 D1 (n= 95, 37)	29.579 (± 4.186)	31.027 (± 3.790)		
C15 D1 (n= 85, 37)	29.859 (± 4.438)	30.730 (± 3.724)		
C16 D1 (n= 82, 33)	29.683 (± 4.242)	31.515 (± 3.242)		
C17 D1 (n= 78, 30)	29.564 (± 4.695)	31.567 (± 3.884)		
C18 D1 (n= 71, 28)	29.380 (± 4.752)	31.107 (± 4.425)		
C19 D1 (n= 57, 24)	29.737 (± 4.414)	31.417 (± 3.911)		
C20 D1 (n= 45, 21)	29.844 (± 4.527)	30.762 (± 4.122)		
C21 D1 (n= 36, 18)	30.889 (± 3.115)	30.056 (± 4.372)		
C22 D1 (n= 23, 12)	31.696 (± 3.081)	31.000 (± 3.275)		
C23 D1 (n= 14, 7)	31.357 (± 3.388)	31.143 (± 4.413)		
End of treatment (n= 72, 42)	26.556 (± 5.487)	26.786 (± 5.982)		
Follow-up (n= 41, 26)	26.805 (± 6.373)	26.769 (± 6.095)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Functional Assessment of Cancer Therapy Kidney Symptom Index -Disease Related Symptoms (FKSI-DRS): Second-Line Subjects

End point title	Functional Assessment of Cancer Therapy Kidney Symptom Index -Disease Related Symptoms (FKSI-DRS): Second-Line Subjects

End point description:

FKSI-DRS: subset of FKSI which is FACT–Kidney Symptom Index questionnaire used to assess QoL for

subjects diagnosed with renal cell cancer. FKSI contains 15 questions and FKSI-DRS 9 questions (lack of energy, pain, losing weight, bone pain, fatigue, short of breath, coughing, bothered by fevers, hematuria) each ranging from 0 (not at all) to 4 (very much). FKSI-DRS total score 0 to 36; higher scores associated with better health states (Individual questions may be reversed coded, as appropriate). FAS previously-treated Asian population. Here 'Number of subjects analysed' signifies those subjects who were evaluable for this endpoint and 'n' signifies those subjects evaluated for this endpoint at specific time points for each group respectively.

End point type	Other pre-specified

End point timeframe:

Baseline (Pre-dose on Cycle [C]1 Day [D]1), D1 of each cycle until C21, end of treatment (up to Week 103), follow-up (28 days after last dose)

End point values	Axitinib (Second-line Subjects): PCD	Sorafenib (Second-line Subjects): PCD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	134	69		
Units: units on a scale				
arithmetic mean (standard deviation)				
C1 D1 (n= 134, 69)	31.020 (± 3.986)	31.489 (± 4.538)		
C2 D1 (n= 127, 66)	30.600 (± 3.892)	30.682 (± 3.895)		
C3 D1 (n= 124, 57)	30.645 (± 3.681)	30.965 (± 3.803)		
C4 D1 (n= 116, 53)	30.103 (± 4.558)	30.679 (± 3.980)		
C5 D1 (n= 111, 48)	30.676 (± 4.271)	31.063 (± 3.629)		
C6 D1 (n= 108, 41)	30.731 (± 3.973)	31.439 (± 4.249)		
C7 D1 (n= 100, 38)	30.920 (± 4.373)	30.632 (± 4.365)		
C8 D1 (n= 89, 37)	30.966 (± 4.144)	30.703 (± 5.195)		
C9 D1 (n= 82, 33)	31.012 (± 3.783)	30.667 (± 4.884)		
C10 D1 (n= 74, 27)	30.986 (± 4.133)	30.926 (± 4.215)		
C11 D1 (n= 66, 22)	31.212 (± 4.033)	32.045 (± 3.579)		
C12 D1 (n= 59, 22)	31.356 (± 3.443)	32.000 (± 3.338)		
C13 D1 (n= 55, 20)	31.418 (± 3.775)	32.100 (± 2.989)		
C14 D1 (n= 50, 15)	32.100 (± 3.321)	32.800 (± 2.274)		
C15 D1 (n= 44, 13)	32.000 (± 2.861)	32.769 (± 2.279)		
C16 D1 (n= 38, 12)	31.921 (± 3.372)	33.167 (± 2.167)		
C17 D1 (n= 33, 10)	32.061 (± 3.344)	32.800 (± 2.898)		
C18 D1 (n= 29, 8)	31.931 (± 3.116)	32.625 (± 2.615)		
C19 D1 (n= 22, 7)	32.364 (± 2.341)	32.429 (± 4.429)		

C20 D1 (n= 21, 6)	31.905 (± 2.998)	33.500 (± 2.168)		
C21 D1 (n= 16, 6)	33.125 (± 2.473)	33.500 (± 2.345)		
End of treatment (n= 37, 27)	28.216 (± 5.662)	29.519 (± 4.661)		
Follow-up (n= 13, 12)	24.692 (± 4.366)	27.500 (± 6.762)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Euro Quality of Life Questionnaire- 5 Dimensions (EQ-5D) Index Score: First-Line Subjects

End point title	Euro Quality of Life Questionnaire- 5 Dimensions (EQ-5D) Index Score: First-Line Subjects

End point description:

EQ-5D: Subject rated questionnaire to assess health-related quality of life in terms of a single utility score. Health State Profile component assesses level of current health for 5 domains: mobility, self-care, usual activities, pain and discomfort, and anxiety and depression; 1 indicates better health state (no problems); 3 indicates worst health state ("confined to bed"). Scoring formula developed by EuroQol Group assigns a utility value for each domain in the profile. Score is transformed and results in a total score range -0.594 to 1.000; higher score indicates a better health state. FAS treatment-naive population. Here 'Number of subjects analysed' signifies those subjects who were evaluable for this endpoint and 'n' signifies those subjects evaluated for this endpoint at specific time points for each group respectively.

End point type	Other pre-specified

End point timeframe:

Baseline (Pre-dose on Cycle [C]1 Day [D]1), D1 of each cycle until C23, end of treatment (up to Week 107), follow-up (28 days after last dose)

End point values	Axitinib (First-line Subjects): PCD	Sorafenib (First-line Subjects): PCD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	183	94		
Units: units on a scale				
arithmetic mean (standard deviation)				
C1 D1 (n= 183, 94)	0.710 (± 0.254)	0.712 (± 0.272)		
C2 D1 (n= 175, 90)	0.709 (± 0.214)	0.693 (± 0.237)		
C3 D1 (n= 163, 84)	0.694 (± 0.251)	0.687 (± 0.261)		
C4 D1 (n= 156, 81)	0.696 (± 0.235)	0.668 (± 0.265)		
C5 D1 (n= 153, 77)	0.708 (± 0.221)	0.673 (± 0.269)		
C6 D1 (n= 140, 72)	0.683 (± 0.263)	0.641 (± 0.281)		
C7 D1 (n= 139, 65)	0.685 (± 0.225)	0.676 (± 0.676)		

C8 D1 (n= 131, 60)	0.678 (± 0.274)	0.717 (± 0.244)		
C9 D1 (n= 126, 59)	0.704 (± 0.239)	0.729 (± 0.202)		
C10 D1 (n= 122, 55)	0.682 (± 0.277)	0.723 (± 0.238)		
C11 D1 (n= 114, 48)	0.698 (± 0.260)	0.748 (± 0.199)		
C12 D1 (n= 105, 44)	0.708 (± 0.227)	0.742 (± 0.218)		
C13 D1 (n= 99, 44)	0.708 (± 0.253)	0.761 (± 0.220)		
C14 D1 (n= 95, 37)	0.703 (± 0.260)	0.731 (± 0.254)		
C15 D1 (n= 85, 37)	0.689 (± 0.269)	0.755 (± 0.225)		
C16 D1 (n= 82, 33)	0.702 (± 0.244)	0.775 (± 0.186)		
C17 D1 (n= 78, 30)	0.706 (± 0.250)	0.738 (± 0.250)		
C18 D1 (n= 71, 28)	0.699 (± 0.259)	0.777 (± 0.191)		
C19 D1 (n= 56, 24)	0.713 (± 0.256)	0.762 (± 0.261)		
C20 D1 (n= 45, 21)	0.699 (± 0.261)	0.710 (± 0.300)		
C21 D1 (n= 36, 18)	0.712 (± 0.232)	0.702 (± 0.307)		
C22 D1 (n= 23, 12)	0.737 (± 0.255)	0.774 (± 0.177)		
C23 D1 (n= 14, 7)	0.736 (± 0.275)	0.789 (± 0.187)		
End of treatment (n= 70, 42)	0.635 (± 0.268)	0.588 (± 0.291)		
Follow-up (n= 41, 26)	0.545 (± 0.434)	0.618 (± 0.254)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Euro Quality of Life Questionnaire- 5 Dimensions (EQ-5D) Index Score: Second-Line Subjects

End point title	Euro Quality of Life Questionnaire- 5 Dimensions (EQ-5D) Index Score: Second-Line Subjects

End point description:

EQ-5D: Subject rated questionnaire to assess health-related quality of life in terms of a single utility score. Health State Profile component assesses level of current health for 5 domains: mobility, self-care, usual activities, pain and discomfort, and anxiety and depression; 1 indicates better health state (no problems); 3 indicates worst health state ("confined to bed"). Scoring formula developed by EuroQol Group assigns a utility value for each domain in the profile. Score is transformed and results in a total score range -0.594 to 1.000; higher score indicates a better health state. FAS previously-treated Asian population. Here 'Number of subjects analysed' signifies those subjects who were evaluable for this endpoint and 'n' signifies those subjects evaluated for this endpoint at specific time points for each group respectively.

End point type	Other pre-specified

End point timeframe:

Baseline (Pre-dose on Cycle [C]1 Day [D]1), D1 of each cycle until C21, end of treatment (up to Week

End point values	Axitinib (Second-line Subjects): PCD	Sorafenib (Second-line Subjects): PCD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	134	69		
Units: units on a scale				
arithmetic mean (standard deviation)				
C1 D1 (n= 134, 69)	0.812 (± 0.225)	0.831 (± 0.186)		
C2 D1 (n= 127, 65)	0.769 (± 0.218)	0.754 (± 0.251)		
C3 D1 (n= 124, 58)	0.772 (± 0.206)	0.755 (± 0.278)		
C4 D1 (n= 116, 53)	0.737 (± 0.272)	0.759 (± 0.211)		
C5 D1 (n= 111, 48)	0.780 (± 0.203)	0.768 (± 0.275)		
C6 D1 (n= 108, 41)	0.767 (± 0.251)	0.753 (± 0.245)		
C7 D1 (n= 100, 38)	0.762 (± 0.252)	0.768 (± 0.239)		
C8 D1 (n= 89, 37)	0.758 (± 0.241)	0.733 (± 0.339)		
C9 D1 (n= 82, 33)	0.796 (± 0.203)	0.794 (± 0.262)		
C10 D1 (n= 74, 27)	0.768 (± 0.243)	0.820 (± 0.169)		
C11 D1 (n= 66, 22)	0.792 (± 0.210)	0.848 (± 0.158)		
C12 D1 (n= 59, 22)	0.797 (± 0.201)	0.837 (± 0.157)		
C13 D1 (n= 55, 20)	0.786 (± 0.217)	0.814 (± 0.156)		
C14 D1 (n= 50, 15)	0.833 (± 0.162)	0.871 (± 0.131)		
C15 D1 (n= 44, 13)	0.819 (± 0.151)	0.829 (± 0.152)		
C16 D1 (n= 38, 12)	0.811 (± 0.186)	0.828 (± 0.142)		
C17 D1 (n= 33, 10)	0.834 (± 0.158)	0.865 (± 0.122)		
C18 D1 (n= 29, 8)	0.830 (± 0.164)	0.829 (± 0.160)		
C19 D1 (n= 22, 7)	0.830 (± 0.148)	0.861 (± 0.139)		
C20 D1 (n= 21, 6)	0.832 (± 0.163)	0.923 (± 0.129)		
C21 D1 (n= 16, 6)	0.859 (± 0.155)	0.852 (± 0.176)		
End of treatment (n= 37, 27)	0.582 (± 0.406)	0.623 (± 0.296)		
Follow-up (n= 13, 12)	0.429 (± 0.358)	0.418 (± 0.565)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Euro Quality of Life Questionnaire- 5 Dimensions (EQ-5D) Visual Analog Scale (VAS): First-Line Subjects

End point title	Euro Quality of Life Questionnaire- 5 Dimensions (EQ-5D) Visual Analog Scale (VAS): First-Line Subjects

End point description:

EQ-5D: Subject rated questionnaire to assess health-related quality of life in terms of a single index value. The VAS component rates current health state on a scale from 0: worst imaginable health state to 100: best imaginable health state; higher scores indicate a better health state. FAS treatment-naive population. Here 'Number of subjects analysed' signifies those subjects who were evaluable for this endpoint and 'n' signifies those subjects evaluated for this endpoint at specific time points for each group respectively.

End point type	Other pre-specified

End point timeframe:

Baseline (Pre-dose on Cycle [C]1 Day [D]1), D1 of each cycle until C23, end of treatment (up to Week 107), follow-up (28 days after last dose)

End point values	Axitinib (First-line Subjects): PCD	Sorafenib (First-line Subjects): PCD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	182	94		
Units: units on a scale				
arithmetic mean (standard deviation)				
C1 D1 (n= 182, 94)	71.181 (± 19.641)	72.362 (± 16.466)		
C2 D1 (n= 175, 90)	71.714 (± 16.583)	72.422 (± 14.576)		
C3 D1 (n= 165, 83)	72.006 (± 16.971)	71.241 (± 16.252)		
C4 D1 (n= 156, 81)	72.179 (± 16.980)	72.086 (± 14.904)		
C5 D1 (n= 153, 78)	72.451 (± 18.237)	73.615 (± 14.665)		
C6 D1 (n= 141, 72)	71.574 (± 18.929)	69.944 (± 17.535)		
C7 D1 (n= 139, 65)	71.050 (± 18.967)	73.923 (± 13.998)		
C8 D1 (n= 131, 60)	71.031 (± 19.081)	73.183 (± 16.674)		
C9 D1 (n= 126, 59)	72.690 (± 18.789)	73.780 (± 16.180)		
C10 D1 (n= 122, 55)	72.910 (± 19.354)	72.400 (± 18.814)		
C11 D1 (n= 114, 48)	72.763 (± 18.174)	72.271 (± 18.512)		

C12 D1 (n= 105, 44)	73.610 (± 18.275)	75.295 (± 17.052)		
C13 D1 (n= 99, 44)	73.030 (± 18.348)	75.432 (± 17.907)		
C14 D1 (n= 95, 37)	73.147 (± 17.546)	75.108 (± 18.371)		
C15 D1 (n= 85, 37)	74.494 (± 17.938)	74.405 (± 17.650)		
C16 D1 (n= 82, 33)	73.878 (± 18.289)	75.818 (± 17.716)		
C17 D1 (n= 78, 30)	73.090 (± 17.717)	74.333 (± 18.654)		
C18 D1 (n= 71, 28)	73.817 (± 17.288)	75.571 (± 18.550)		
C19 D1 (n= 56, 24)	72.089 (± 18.169)	75.125 (± 20.919)		
C20 D1 (n= 45, 21)	74.244 (± 17.044)	74.190 (± 20.425)		
C21 D1 (n= 36, 18)	75.694 (± 11.918)	70.500 (± 21.637)		
C22 D1 (n= 23, 12)	78.000 (± 12.544)	73.917 (± 15.900)		
C23 D1 (n= 14, 7)	77.143 (± 12.697)	72.571 (± 14.820)		
End of treatment (n= 71, 42)	67.254 (± 19.495)	67.048 (± 22.570)		
Follow-up (n= 41, 26)	69.195 (± 20.366)	64.885 (± 19.916)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Euro Quality of Life Questionnaire- 5 Dimensions (EQ-5D) Visual Analog Scale (VAS): Second-Line Subjects

End point title	Euro Quality of Life Questionnaire- 5 Dimensions (EQ-5D) Visual Analog Scale (VAS): Second-Line Subjects

End point description:

EQ-5D: Subject rated questionnaire to assess health-related quality of life in terms of a single index value. The VAS component rates current health state on a scale from 0: worst imaginable health state to 100: best imaginable health state; higher scores indicate a better health state. FAS previously-treated Asian population. Here 'Number of subjects analysed' signifies those subjects who were evaluable for this endpoint and 'n' signifies those endpoint evaluated for this measure at specific time points for each group respectively.

End point type	Other pre-specified

End point timeframe:

Baseline (Pre-dose on Cycle [C]1 Day [D]1), D1 of each cycle until C21, end of treatment (up to Week 103), follow-up (28 days after last dose)

End point values	Axitinib (Second-line Subjects): PCD	Sorafenib (Second-line Subjects): PCD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	134	69		
Units: units on a scale				
arithmetic mean (standard deviation)				
C1 D1 (n= 134, 69)	82.799 (± 13.351)	82.058 (± 14.021)		
C2 D1 (n= 127, 65)	81.102 (± 13.895)	78.231 (± 15.823)		
C3 D1 (n= 124, 58)	80.895 (± 13.387)	80.534 (± 16.453)		
C4 D1 (n= 116, 53)	81.138 (± 13.508)	81.245 (± 14.590)		
C5 D1 (n= 111, 48)	83.018 (± 12.829)	80.250 (± 15.495)		
C6 D1 (n= 108, 41)	82.222 (± 13.793)	80.829 (± 15.091)		
C7 D1 (n= 100, 38)	82.900 (± 13.287)	80.868 (± 16.140)		
C8 D1 (n= 89, 37)	83.382 (± 12.636)	81.000 (± 14.606)		
C9 D1 (n= 82, 33)	84.171 (± 11.260)	83.788 (± 10.349)		
C10 D1 (n= 74, 27)	83.041 (± 13.042)	82.778 (± 11.440)		
C11 D1 (n= 66, 22)	84.136 (± 14.231)	83.000 (± 11.832)		
C12 D1 (n= 59, 22)	84.305 (± 13.211)	83.500 (± 12.188)		
C13 D1 (n= 55, 20)	82.927 (± 17.317)	83.300 (± 11.263)		
C14 D1 (n= 50, 15)	86.520 (± 10.831)	86.667 (± 8.715)		
C15 D1 (n= 44, 13)	85.841 (± 11.783)	86.462 (± 8.678)		
C16 D1 (n= 38, 12)	87.579 (± 10.391)	86.083 (± 8.816)		
C17 D1 (n= 33, 10)	88.424 (± 10.866)	84.300 (± 10.328)		
C18 D1 (n= 29, 8)	86.586 (± 13.605)	83.125 (± 8.839)		
C19 D1 (n= 22, 7)	89.500 (± 8.684)	82.143 (± 11.495)		
C20 D1 (n= 21, 6)	90.333 (± 8.679)	86.000 (± 9.695)		
C21 D1 (n= 16, 6)	90.313 (± 9.741)	84.167 (± 9.704)		
End of treatment (n= 37, 27)	75.568 (± 17.934)	74.741 (± 17.623)		
Follow-up (n= 13, 12)	58.154 (± 20.760)	64.333 (± 25.564)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to at least 3 years after the randomization of the last subject

Adverse event reporting additional description:

Same event may appear as both adverse event(AE) and serious AE(SAE). What is presented are distinct events. An event may be categorised as serious in 1 subject and as non-serious in another, or a subject may have experienced both serious and non-serious event. Safety analysis set. Safety reported for all subjects excluding subjects from China.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Axitinib (Second-line Subjects)

Reporting group description:

Asian subjects with prior systemic first-line therapy containing sunitinib or cytokine received axitinib (AG-013736) tablet at a starting dose of 5 mg orally twice daily, dose adjustment was done based on the tolerability, as per investigator’s discretion. Study medication was administered in cycles of 4 weeks.

Reporting group title	Sorafenib (Second-line Subjects)

Reporting group description:

Asian subjects with prior systemic first-line therapy containing sunitinib or cytokine received sorafenib tablet at a starting dose of 400 mg orally twice daily, dose adjustment was done based on the tolerability, as per investigator’s discretion. Study medication was administered in cycles of 4 weeks.

Reporting group title	Axitinib (First-line Subjects)

Reporting group description:

Subjects with no prior systemic first-line therapy received axitinib (AG-013736) tablet at a starting dose of 5 mg orally twice daily, dose adjustment was done based on the tolerability, as per investigator’s discretion. Study medication was administered in cycles of 4 weeks.

Reporting group title	Sorafenib (First-line Subjects)

Reporting group description:

Subjects with no prior systemic first-line therapy received sorafenib tablet at a starting dose of 400 mg orally twice daily, dose adjustment was done based on the tolerability, as per investigator’s discretion. Study medication was administered in cycles of 4 weeks.

Serious adverse events	Axitinib (Second-line Subjects)	Sorafenib (Second-line Subjects)	Axitinib (First-line Subjects)
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 11 (54.55%)	3 / 5 (60.00%)	77 / 173 (44.51%)
number of deaths (all causes)	9	3	117
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cardiac neoplasm unspecified			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal cancer			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	2 / 173 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Renal cancer metastatic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	2 / 173 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Renal cell carcinoma			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Malignant neoplasm progression			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	3 / 173 (1.73%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Angiopathy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration			

site conditions			
Death			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disease progression			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	20 / 173 (11.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 20
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 20
Asthenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	2 / 173 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	2 / 173 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Impaired healing			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			

subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	2 / 173 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pulmonary embolism			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	2 / 173 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Atelectasis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			

subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory distress			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory failure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Haemoglobin decreased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Facial bones fracture			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple injuries			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Patella fracture			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	2 / 173 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Angina pectoris			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	3 / 173 (1.73%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Acute myocardial infarction			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Atrial flutter			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	3 / 173 (1.73%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 3
Cardio-respiratory arrest			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	2 / 173 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Atrioventricular block second degree			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cardiomyopathy			

subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Axonal and demyelinating polyneuropathy			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic stroke			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cerebral ischaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraparesis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			

subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 11 (27.27%)	1 / 5 (20.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 11 (18.18%)	1 / 5 (20.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	1 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	8 / 173 (4.62%)
occurrences causally related to treatment / all	1 / 2	0 / 0	6 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			

subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal distension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Impaired gastric emptying			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Melaena			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			

subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peptic ulcer			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	3 / 173 (1.73%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retroperitoneal haematoma			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortoenteric fistula			

subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Erythema multiforme			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Ureteric obstruction			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysuria			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Urinary retention			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cholecystitis infective			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 11 (9.09%)	1 / 5 (20.00%)	4 / 173 (2.31%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pyelonephritis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	2 / 173 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Skin bacterial infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	2 / 173 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			

subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Sorafenib (First-line Subjects)		
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 88 (29.55%)		
number of deaths (all causes)	63		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cardiac neoplasm unspecified			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal cancer			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal cancer metastatic			

subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal cell carcinoma				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Tumour haemorrhage				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant neoplasm progression				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung neoplasm malignant				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Angiopathy				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypertensive crisis				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Death				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Disease progression			
subjects affected / exposed	6 / 88 (6.82%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 6		
Asthenia			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chest pain			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Impaired healing			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Mucosal inflammation			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sudden death			

subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Epistaxis			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	3 / 88 (3.41%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atelectasis			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemoptysis			

subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pleurisy				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary oedema				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory distress				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Haemoglobin decreased				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Ankle fracture				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Facial bones fracture				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Humerus fracture				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multiple injuries				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Patella fracture				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Upper limb fracture				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Wound dehiscence				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Contusion				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Angina pectoris				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				

subjects affected / exposed	2 / 88 (2.27%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Myocardial ischaemia				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	2 / 88 (2.27%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Atrial flutter				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardio-respiratory arrest				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrioventricular block second degree				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic cardiomyopathy				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Axonal and demyelinating polyneuropathy				

subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemorrhagic stroke				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral haemorrhage				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral ischaemia				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Paraparesis				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal cord compression				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				

subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 88 (3.41%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Anal fistula			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	2 / 88 (2.27%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oesophagitis			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper gastrointestinal haemorrhage			

subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal distension				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastric haemorrhage				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastric ulcer				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Impaired gastric emptying				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Melaena				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Oesophageal varices haemorrhage				

subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peptic ulcer				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Proctitis				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal haemorrhage				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Retroperitoneal haematoma				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal pain upper				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aortoenteric fistula				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis				

subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis acute				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Erythema multiforme				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Palmar-plantar erythrodysaesthesia syndrome				
subjects affected / exposed	2 / 88 (2.27%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Ureteric obstruction				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dysuria				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematuria				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary retention				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Muscular weakness			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pathological fracture			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abscess			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholecystitis infective			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Pneumonia				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin bacterial infection				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Tonsillitis				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound infection				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal abscess				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				

Decreased appetite			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperkalaemia			
subjects affected / exposed	2 / 88 (2.27%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Axitinib (Second-line Subjects)	Sorafenib (Second-line Subjects)	Axitinib (First-line Subjects)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 11 (100.00%)	5 / 5 (100.00%)	161 / 173 (93.06%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anal neoplasm			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	0 / 173 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 11 (36.36%)	1 / 5 (20.00%)	83 / 173 (47.98%)
occurrences (all)	11	3	242
Hypotension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	13 / 173 (7.51%)
occurrences (all)	0	0	18
Surgical and medical procedures			
Haemostasis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			

Chest pain			
subjects affected / exposed	1 / 11 (9.09%)	1 / 5 (20.00%)	9 / 173 (5.20%)
occurrences (all)	1	1	15
Fatigue			
subjects affected / exposed	4 / 11 (36.36%)	2 / 5 (40.00%)	55 / 173 (31.79%)
occurrences (all)	7	2	121
Pyrexia			
subjects affected / exposed	2 / 11 (18.18%)	0 / 5 (0.00%)	9 / 173 (5.20%)
occurrences (all)	2	0	10
Asthenia			
subjects affected / exposed	5 / 11 (45.45%)	0 / 5 (0.00%)	41 / 173 (23.70%)
occurrences (all)	6	0	67
Mucosal inflammation			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	21 / 173 (12.14%)
occurrences (all)	1	0	42
Oedema peripheral			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	10 / 173 (5.78%)
occurrences (all)	1	0	15
Reproductive system and breast disorders			
Breast mass			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	0 / 173 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 11 (18.18%)	1 / 5 (20.00%)	33 / 173 (19.08%)
occurrences (all)	2	2	44
Dysphonia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	37 / 173 (21.39%)
occurrences (all)	0	0	49
Dyspnoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	24 / 173 (13.87%)
occurrences (all)	0	0	32
Pleural effusion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	3 / 173 (1.73%)
occurrences (all)	0	0	3
Epistaxis			

subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	7 / 173 (4.05%)
occurrences (all)	0	0	8
Oropharyngeal pain			
subjects affected / exposed	4 / 11 (36.36%)	0 / 5 (0.00%)	12 / 173 (6.94%)
occurrences (all)	5	0	20
Dry throat			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	10 / 173 (5.78%)
occurrences (all)	0	0	14
Insomnia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	10 / 173 (5.78%)
occurrences (all)	1	0	13
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	19 / 173 (10.98%)
occurrences (all)	0	0	36
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	17 / 173 (9.83%)
occurrences (all)	0	0	27
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	7 / 173 (4.05%)
occurrences (all)	0	0	14
Blood creatinine increased			
subjects affected / exposed	2 / 11 (18.18%)	1 / 5 (20.00%)	14 / 173 (8.09%)
occurrences (all)	9	2	29
Blood phosphorus decreased			
subjects affected / exposed	1 / 11 (9.09%)	1 / 5 (20.00%)	0 / 173 (0.00%)
occurrences (all)	2	2	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	17 / 173 (9.83%)
occurrences (all)	1	0	20
Lipase increased			

subjects affected / exposed	2 / 11 (18.18%)	1 / 5 (20.00%)	7 / 173 (4.05%)
occurrences (all)	5	1	25
Weight decreased			
subjects affected / exposed	4 / 11 (36.36%)	1 / 5 (20.00%)	70 / 173 (40.46%)
occurrences (all)	13	1	198
Amylase increased			
subjects affected / exposed	3 / 11 (27.27%)	1 / 5 (20.00%)	0 / 173 (0.00%)
occurrences (all)	4	2	0
Blood bicarbonate decreased			
subjects affected / exposed	1 / 11 (9.09%)	1 / 5 (20.00%)	0 / 173 (0.00%)
occurrences (all)	3	1	0
Blood bilirubin increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	3	0	0
Blood calcium increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Blood chloride increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Blood cholesterol increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	0 / 173 (0.00%)
occurrences (all)	0	1	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	0 / 173 (0.00%)
occurrences (all)	0	1	0
Blood urea increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	0 / 173 (0.00%)
occurrences (all)	0	1	0
Glomerular filtration rate decreased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Creatinine renal clearance decreased			
subjects affected / exposed	2 / 11 (18.18%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	3	0	0

Eosinophil count increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	2	0	0
Haematocrit increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Haemoglobin decreased			
subjects affected / exposed	2 / 11 (18.18%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	2	0	0
Haemoglobin increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Liver function test increased			
subjects affected / exposed	1 / 11 (9.09%)	2 / 5 (40.00%)	0 / 173 (0.00%)
occurrences (all)	1	2	0
International normalised ratio increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	0 / 173 (0.00%)
occurrences (all)	0	1	0
Lymphocyte percentage decreased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	0 / 173 (0.00%)
occurrences (all)	0	2	0
Protein total decreased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	2	0	0
Tri-iodothyronine free decreased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	3	0	0
Blood pressure increased			
subjects affected / exposed	2 / 11 (18.18%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	4	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	10 / 173 (5.78%)
occurrences (all)	2	0	12
Mucosal excoriation			

subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Skin abrasion			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Spinal compression fracture			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	14 / 173 (8.09%)
occurrences (all)	2	0	22
Headache			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	23 / 173 (13.29%)
occurrences (all)	1	0	42
Dizziness exertional			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Dysaesthesia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Neuralgia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	0 / 173 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 11 (18.18%)	2 / 5 (40.00%)	15 / 173 (8.67%)
occurrences (all)	8	6	30
Anisocytosis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Macrocytosis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	3	0	0
Polychromasia			

subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Thrombocytopenia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Thrombocytosis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	0 / 173 (0.00%)
occurrences (all)	0	6	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 11 (27.27%)	0 / 5 (0.00%)	17 / 173 (9.83%)
occurrences (all)	7	0	72
Abdominal pain upper			
subjects affected / exposed	2 / 11 (18.18%)	0 / 5 (0.00%)	32 / 173 (18.50%)
occurrences (all)	2	0	51
Constipation			
subjects affected / exposed	2 / 11 (18.18%)	1 / 5 (20.00%)	17 / 173 (9.83%)
occurrences (all)	2	1	25
Diarrhoea			
subjects affected / exposed	6 / 11 (54.55%)	2 / 5 (40.00%)	88 / 173 (50.87%)
occurrences (all)	16	3	495
Mouth ulceration			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	38 / 173 (21.97%)
occurrences (all)	2	0	138
Stomatitis			

subjects affected / exposed	2 / 11 (18.18%)	1 / 5 (20.00%)	20 / 173 (11.56%)
occurrences (all)	3	2	60
Vomiting			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	38 / 173 (21.97%)
occurrences (all)	0	0	176
Abdominal distension			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	9 / 173 (5.20%)
occurrences (all)	1	0	11
Dry mouth			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	10 / 173 (5.78%)
occurrences (all)	0	0	13
Dyspepsia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	13 / 173 (7.51%)
occurrences (all)	1	0	15
Flatulence			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	10 / 173 (5.78%)
occurrences (all)	0	0	11
Abdominal discomfort			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	0 / 173 (0.00%)
occurrences (all)	0	1	0
Anal fissure			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	0 / 173 (0.00%)
occurrences (all)	0	1	0
Cheilitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Duodenitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Gastric ulcer			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Gingival bleeding			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			

subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Glossodynia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Haematemesis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Haemorrhoids			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Hiatus hernia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Hyperchlorhydria			
subjects affected / exposed	2 / 11 (18.18%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	2	0	0
Melaena			
subjects affected / exposed	2 / 11 (18.18%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	2	0	0
Oesophagitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Oral disorder			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Rectal haemorrhage			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	4	0	0
Toothache			
subjects affected / exposed	2 / 11 (18.18%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	2	0	0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	0 / 173 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	1 / 11 (9.09%)	1 / 5 (20.00%)	6 / 173 (3.47%)
occurrences (all)	1	4	8
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	4 / 11 (36.36%)	4 / 5 (80.00%)	41 / 173 (23.70%)
occurrences (all)	17	8	206
Rash			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	15 / 173 (8.67%)
occurrences (all)	2	0	19
Erythema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	5 / 173 (2.89%)
occurrences (all)	0	0	6
Pruritus			
subjects affected / exposed	1 / 11 (9.09%)	1 / 5 (20.00%)	7 / 173 (4.05%)
occurrences (all)	1	3	7
Skin exfoliation			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	3 / 173 (1.73%)
occurrences (all)	1	0	3
Blister			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Dry skin			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Pain of skin			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Eczema			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Pigmentation disorder			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Skin fissures			

subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Rash erythematous			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Skin hyperpigmentation			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Skin mass			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	0 / 173 (0.00%)
occurrences (all)	0	1	0
Skin lesion			
subjects affected / exposed	2 / 11 (18.18%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	4	0	0
Skin toxicity			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Skin ulcer			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	3	0	0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	6 / 11 (54.55%)	0 / 5 (0.00%)	19 / 173 (10.98%)
occurrences (all)	34	0	63
Chronic kidney disease			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	0 / 173 (0.00%)
occurrences (all)	0	1	0
Dysuria			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	2	0	0
Haematuria			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Pollakiuria			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0

Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	3 / 11 (27.27%)	0 / 5 (0.00%)	36 / 173 (20.81%)
occurrences (all)	7	0	46
Hyperthyroidism			
subjects affected / exposed	2 / 11 (18.18%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 11 (45.45%)	1 / 5 (20.00%)	28 / 173 (16.18%)
occurrences (all)	7	1	66
Musculoskeletal pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	0 / 173 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	6 / 11 (54.55%)	0 / 5 (0.00%)	29 / 173 (16.76%)
occurrences (all)	11	0	52
Pain in extremity			
subjects affected / exposed	4 / 11 (36.36%)	0 / 5 (0.00%)	23 / 173 (13.29%)
occurrences (all)	5	0	36
Muscle spasms			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	3 / 173 (1.73%)
occurrences (all)	0	0	7
Arthritis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	7 / 173 (4.05%)
occurrences (all)	0	0	8
Flank pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Gouty arthritis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	6	0	0
Myalgia			

subjects affected / exposed	4 / 11 (36.36%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	4	0	0
Osteoarthritis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	2	0	0
Joint swelling			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Periarthritis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 11 (18.18%)	0 / 5 (0.00%)	10 / 173 (5.78%)
occurrences (all)	2	0	10
Upper respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	14 / 173 (8.09%)
occurrences (all)	0	1	18
Urinary tract infection			
subjects affected / exposed	2 / 11 (18.18%)	0 / 5 (0.00%)	10 / 173 (5.78%)
occurrences (all)	2	0	15
Haemorrhoid infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Pharyngotonsillitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Tooth infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0

Tonsillitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	5 / 11 (45.45%)	0 / 5 (0.00%)	48 / 173 (27.75%)
occurrences (all)	5	0	85
Hyperkalaemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Hyperlipidaemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	6 / 173 (3.47%)
occurrences (all)	0	0	12
Hyperuricaemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 173 (0.00%)
occurrences (all)	2	0	0

Non-serious adverse events	Sorafenib (First-line Subjects)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	83 / 88 (94.32%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anal neoplasm			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	28 / 88 (31.82%)		
occurrences (all)	43		
Hypotension			
subjects affected / exposed	3 / 88 (3.41%)		
occurrences (all)	4		
Surgical and medical procedures			
Haemostasis			

subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	7 / 88 (7.95%)		
occurrences (all)	7		
Fatigue			
subjects affected / exposed	25 / 88 (28.41%)		
occurrences (all)	33		
Pyrexia			
subjects affected / exposed	4 / 88 (4.55%)		
occurrences (all)	4		
Asthenia			
subjects affected / exposed	15 / 88 (17.05%)		
occurrences (all)	20		
Mucosal inflammation			
subjects affected / exposed	9 / 88 (10.23%)		
occurrences (all)	11		
Oedema peripheral			
subjects affected / exposed	4 / 88 (4.55%)		
occurrences (all)	5		
Reproductive system and breast disorders			
Breast mass			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	14 / 88 (15.91%)		
occurrences (all)	22		
Dysphonia			
subjects affected / exposed	10 / 88 (11.36%)		
occurrences (all)	10		
Dyspnoea			
subjects affected / exposed	11 / 88 (12.50%)		
occurrences (all)	14		

Pleural effusion subjects affected / exposed occurrences (all)	5 / 88 (5.68%) 5		
Epistaxis subjects affected / exposed occurrences (all)	5 / 88 (5.68%) 5		
Oropharyngeal pain subjects affected / exposed occurrences (all)	5 / 88 (5.68%) 5		
Dry throat subjects affected / exposed occurrences (all)	0 / 88 (0.00%) 0		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	0 / 88 (0.00%) 0		
Insomnia subjects affected / exposed occurrences (all)	5 / 88 (5.68%) 5		
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	8 / 88 (9.09%) 14		
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	8 / 88 (9.09%) 12		
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	6 / 88 (6.82%) 7		
Blood creatinine increased subjects affected / exposed occurrences (all)	6 / 88 (6.82%) 7		
Blood phosphorus decreased subjects affected / exposed occurrences (all)	0 / 88 (0.00%) 0		
Blood thyroid stimulating hormone increased			

subjects affected / exposed	2 / 88 (2.27%)			
occurrences (all)	2			
Lipase increased				
subjects affected / exposed	5 / 88 (5.68%)			
occurrences (all)	9			
Weight decreased				
subjects affected / exposed	24 / 88 (27.27%)			
occurrences (all)	63			
Amylase increased				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			
Blood bicarbonate decreased				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			
Blood bilirubin increased				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			
Blood calcium increased				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			
Blood chloride increased				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			
Blood cholesterol increased				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			
Blood lactate dehydrogenase increased				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			
Blood urea increased				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			
Glomerular filtration rate decreased				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			

Creatinine renal clearance decreased subjects affected / exposed occurrences (all)	0 / 88 (0.00%) 0		
Eosinophil count increased subjects affected / exposed occurrences (all)	0 / 88 (0.00%) 0		
Haematocrit increased subjects affected / exposed occurrences (all)	0 / 88 (0.00%) 0		
Haemoglobin decreased subjects affected / exposed occurrences (all)	0 / 88 (0.00%) 0		
Haemoglobin increased subjects affected / exposed occurrences (all)	0 / 88 (0.00%) 0		
Liver function test increased subjects affected / exposed occurrences (all)	0 / 88 (0.00%) 0		
International normalised ratio increased subjects affected / exposed occurrences (all)	0 / 88 (0.00%) 0		
Lymphocyte percentage decreased subjects affected / exposed occurrences (all)	0 / 88 (0.00%) 0		
Protein total decreased subjects affected / exposed occurrences (all)	0 / 88 (0.00%) 0		
Tri-iodothyronine free decreased subjects affected / exposed occurrences (all)	0 / 88 (0.00%) 0		
Blood pressure increased subjects affected / exposed occurrences (all)	0 / 88 (0.00%) 0		
Injury, poisoning and procedural complications			

Fall			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Mucosal excoriation			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Skin abrasion			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Spinal compression fracture			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 88 (2.27%)		
occurrences (all)	3		
Headache			
subjects affected / exposed	6 / 88 (6.82%)		
occurrences (all)	7		
Dizziness exertional			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Dysaesthesia			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Neuralgia			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	9 / 88 (10.23%)		
occurrences (all)	19		
Anisocytosis			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Macrocytosis			

subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Polychromasia			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Thrombocytopenia			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Thrombocytosis			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	8 / 88 (9.09%)		
occurrences (all)	11		
Abdominal pain upper			
subjects affected / exposed	7 / 88 (7.95%)		
occurrences (all)	9		
Constipation			
subjects affected / exposed	10 / 88 (11.36%)		
occurrences (all)	12		
Diarrhoea			
subjects affected / exposed	34 / 88 (38.64%)		
occurrences (all)	170		
Mouth ulceration			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Nausea			

subjects affected / exposed	15 / 88 (17.05%)			
occurrences (all)	22			
Stomatitis				
subjects affected / exposed	4 / 88 (4.55%)			
occurrences (all)	6			
Vomiting				
subjects affected / exposed	11 / 88 (12.50%)			
occurrences (all)	29			
Abdominal distension				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences (all)	1			
Dry mouth				
subjects affected / exposed	1 / 88 (1.14%)			
occurrences (all)	1			
Dyspepsia				
subjects affected / exposed	3 / 88 (3.41%)			
occurrences (all)	3			
Flatulence				
subjects affected / exposed	3 / 88 (3.41%)			
occurrences (all)	4			
Abdominal discomfort				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			
Anal fissure				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			
Cheilitis				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			
Duodenitis				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			
Gastric ulcer				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			
Gingival bleeding				

subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			
Gastrooesophageal reflux disease				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			
Glossodynia				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			
Haematemesis				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			
Haemorrhoids				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			
Hiatus hernia				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			
Hyperchlorhydria				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			
Melaena				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			
Oesophagitis				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			
Oral disorder				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			
Rectal haemorrhage				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			
Toothache				
subjects affected / exposed	0 / 88 (0.00%)			
occurrences (all)	0			
Upper gastrointestinal haemorrhage				

subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	17 / 88 (19.32%)		
occurrences (all)	20		
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	31 / 88 (35.23%)		
occurrences (all)	79		
Rash			
subjects affected / exposed	18 / 88 (20.45%)		
occurrences (all)	27		
Erythema			
subjects affected / exposed	21 / 88 (23.86%)		
occurrences (all)	27		
Pruritus			
subjects affected / exposed	9 / 88 (10.23%)		
occurrences (all)	13		
Skin exfoliation			
subjects affected / exposed	6 / 88 (6.82%)		
occurrences (all)	7		
Blister			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Pain of skin			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Eczema			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Pigmentation disorder			

subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Skin fissures			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Rash erythematous			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Skin hyperpigmentation			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Skin mass			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Skin lesion			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Skin toxicity			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Skin ulcer			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	9 / 88 (10.23%)		
occurrences (all)	11		
Chronic kidney disease			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Dysuria			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Haematuria			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		

Pollakiuria			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	5 / 88 (5.68%)		
occurrences (all)	5		
Hyperthyroidism			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	10 / 88 (11.36%)		
occurrences (all)	18		
Musculoskeletal pain			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	14 / 88 (15.91%)		
occurrences (all)	17		
Pain in extremity			
subjects affected / exposed	6 / 88 (6.82%)		
occurrences (all)	8		
Muscle spasms			
subjects affected / exposed	6 / 88 (6.82%)		
occurrences (all)	8		
Arthritis			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Musculoskeletal chest pain			
subjects affected / exposed	5 / 88 (5.68%)		
occurrences (all)	6		
Flank pain			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Gouty arthritis			

subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Osteoarthritis			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Joint swelling			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Periarthritis			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 88 (3.41%)		
occurrences (all)	5		
Upper respiratory tract infection			
subjects affected / exposed	1 / 88 (1.14%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	4 / 88 (4.55%)		
occurrences (all)	5		
Haemorrhoid infection			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Pharyngotonsillitis			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		

Tooth infection			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Tonsillitis			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	16 / 88 (18.18%)		
occurrences (all)	21		
Hyperkalaemia			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Hyperlipidaemia			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	5 / 88 (5.68%)		
occurrences (all)	9		
Hyperuricaemia			
subjects affected / exposed	0 / 88 (0.00%)		
occurrences (all)	0		

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Objective of statistical analysis for secondary endpoints:summarize data using descriptive statistics without performing hypothesis testing. All subjects from sites in China are excluded from updated safety reporting due to lack of HGRAC filings.

Notes: