



Clinical trial results:

A prospective international multicenter Phase II study to evaluate the efficacy, safety and quality of life of oral daily pazopanib in patients with advanced and/or metastatic renal cell carcinoma after previous therapy with checkpoint inhibitor treatment

Summary

EudraCT number	2017-000708-10
Trial protocol	CZ DE ES AT GB HU
Global end of trial date	10 August 2021

Results information

Result version number	v1 (current)
This version publication date	31 July 2022
First version publication date	31 July 2022

Trial information

Trial identification

Sponsor protocol code	CPZP034A2410
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03200717
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.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	10 August 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	10 August 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial was to assess the progression-free survival (PFS) based on local investigator assessment.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 November 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	United States: 1
Country: Number of subjects enrolled	Czechia: 9
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Chile: 24
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Argentina: 1
Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	United Kingdom: 7
Worldwide total number of subjects	62
EEA total number of subjects	28

Notes:

Subjects enrolled per age group

In utero	0
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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)	32
From 65 to 84 years	30
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted across 22 centers in 11 countries

Pre-assignment

Screening details:

A total of 87 participants were screened of which 62 participants were enrolled in the this study to receive study treatment.

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	Pazopanib- 2nd line

Arm description:

Participants received pazopanib as 2nd line treatment

Arm type	Experimental
Investigational medicinal product name	Pazopanib
Investigational medicinal product code	PZP034
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

800mg of pazopanib once daily orally

Arm title	Pazopanib- 3rd line
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Arm description:

Participants received pazopanib as 3rd line treatment

Arm type	Experimental
Investigational medicinal product name	Pazopanib
Investigational medicinal product code	PZP034
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

800mg of pazopanib once daily orally

Number of subjects in period 1	Pazopanib- 2nd line	Pazopanib- 3rd line
Started	47	15
Completed	6	0
Not completed	41	15
Adverse event, serious fatal	2	-

Physician decision	3	2
Adverse event, non-fatal	11	8
Subject/Guardian Decision	1	-
Progressive disease	24	5

Baseline characteristics

Reporting groups

Reporting group title	Pazopanib- 2nd line
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Reporting group description:

Participants received pazopanib as 2nd line treatment

Reporting group title	Pazopanib- 3rd line
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Reporting group description:

Participants received pazopanib as 3rd line treatment

Reporting group values	Pazopanib- 2nd line	Pazopanib- 3rd line	Total
Number of subjects	47	15	62
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	26	6	32
From 65-84 years	21	9	30
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	62.4	65.4	
standard deviation	± 11.55	± 9.77	-
Sex: Female, Male			
Units: Participants			
Female	11	4	15
Male	36	11	47
Race/Ethnicity, Customized			
Units: Subjects			
White	44	13	57
Asian	1	0	1
Other	0	1	1
Unknown	2	1	3

Subject analysis sets

Subject analysis set title	All participants
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Subject analysis set type	Full analysis
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Subject analysis set description:

All participants who received pazopanib as 2nd or 3rd line treatment

Reporting group values	All participants		
Number of subjects	62		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	32		
From 65-84 years	30		
85 years and over	0		
Age Continuous			
Units: Years			
arithmetic mean	63.2		
standard deviation	± 11.15		
Sex: Female, Male			
Units: Participants			
Female	47		
Male	15		
Race/Ethnicity, Customized			
Units: Subjects			
White	57		
Asian	3		
Other	1		
Unknown	1		

End points

End points reporting groups

Reporting group title	Pazopanib- 2nd line
Reporting group description:	
Participants received pazopanib as 2nd line treatment	
Reporting group title	Pazopanib- 3rd line
Reporting group description:	
Participants received pazopanib as 3rd line treatment	
Subject analysis set title	All participants
Subject analysis set type	Full analysis
Subject analysis set description:	
All participants who received pazopanib as 2nd or 3rd line treatment	

Primary: Progression free survival (PFS)

End point title	Progression free survival (PFS) ^[1]
End point description:	
PFS is defined as the time from the start date of pazopanib treatment to the date of the first documented progression or death due to any cause. PFS was assessed via local review according to RECIST 1.1.	
PFS was censored at the date of the last adequate tumor assessment if no PFS event (disease progression or death due to any cause) was observed prior to the analysis cut-off date.	
The PFS distribution was estimated using the Kaplan-Meier method.	
End point type	Primary
End point timeframe:	
Date of first treatment to date of progression or death up to approximately 38 months	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses were planned for this endpoint

End point values	Pazopanib- 2nd line	Pazopanib- 3rd line	All participants	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	47	15	62	
Units: Months				
median (confidence interval 95%)	7.5 (3.7 to 12.6)	4.6 (3.3 to 9.2)	6.8 (3.7 to 11.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall response rate (ORR) based on local investigator assessment according to RECIST v1.1

End point title	Overall response rate (ORR) based on local investigator assessment according to RECIST v1.1
End point description:	
ORR is defined as the percentage of participants with best overall response of confirmed complete response (CR) or partial response (PR) based on local investigator's assessment according to RECIST v1.1. The 95% confidence intervals (CIs) were computed using Clopper and Pearson method.	

CR: Disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm.

PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.

End point type	Secondary
End point timeframe:	
Up to approximately 38 months	

End point values	Pazopanib- 2nd line	Pazopanib- 3rd line	All participants	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	47	15	62	
Units: Percentage of participants				
number (confidence interval 95%)	23.4 (12.3 to 38.0)	0 (0.0 to 21.8)	17.7 (9.2 to 29.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical benefit rate (CBR) based on local investigator assessment according to RECIST v1.1.

End point title	Clinical benefit rate (CBR) based on local investigator assessment according to RECIST v1.1.
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End point description:

CBR is defined as the percentage of participants with a best overall response of CR or PR or an overall lesion response of stable disease (SD) or Non-CR/Non-PD lasting ≥ 24 weeks based on local investigator's assessment according to RECIST v1.1. The 95% confidence intervals (CIs) were computed using Clopper and Pearson method.

CR: Disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm.

PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.

SD: Neither sufficient shrinkage to qualify for PR or CR nor an increase in lesions which would qualify for progressive disease.

End point type	Secondary
End point timeframe:	
Up to approximately 38 months	

End point values	Pazopanib- 2nd line	Pazopanib- 3rd line	All participants	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	47	15	62	
Units: Percentage of participants				
number (confidence interval 95%)	53.2 (38.1 to 67.9)	40.0 (16.3 to 67.7)	50.0 (37.0 to 63.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)
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End point description:

OS is defined as the time from the first administration of study treatment until death due to any cause. If a participant was not known to have died, survival was censored at the date of last known date patient alive.

The OS distribution was estimated using the Kaplan-Meier method.

999 indicates data was not evaluable

End point type	Secondary
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End point timeframe:

From date of first treatment to date of death, up to approximately 44 months

End point values	Pazopanib- 2nd line	Pazopanib- 3rd line	All participants	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	47	15	62	
Units: Months				
median (confidence interval 95%)	27.8 (14.9 to 999)	20.0 (9.2 to 25.6)	23.4 (14.9 to 31.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DOR) based on local Investigators assessment according to RECIST v1.1

End point title	Duration of response (DOR) based on local Investigators assessment according to RECIST v1.1
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End point description:

DOR is defined as the time from the date of first documented response (confirmed CR or PR according to RECIST v1.1 based on local Investigators review of tumor assessment data) to the date of tumor progression, or death due to underlying cancer, whichever comes first.

If a patient not had an event, duration was censored at the date of last adequate tumor assessment.

The DOR distribution was calculated using the Kaplan-Meier method.

999 indicates data was not evaluable

End point type	Secondary
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End point timeframe:

From the date of first documented response (confirmed CR or PR) to the date of tumor progression, up to approximately 36 months

End point values	Pazopanib- 2nd line	Pazopanib- 3rd line		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	0 ^[2]		
Units: Months				
median (confidence interval 95%)	999 (9.5 to 999)	(to)		

Notes:

[2] - No participant had an event (CR or PR)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Functional Assessment of Cancer Therapy- Kidney Symptom (FKSI-DRS) score

End point title	Change from baseline in Functional Assessment of Cancer Therapy- Kidney Symptom (FKSI-DRS) score
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End point description:

FKSI-DRS is a 9-item questionnaire specifically designed to evaluate symptoms that are directly attributable to kidney cancer and includes patient's symptoms in the past seven days such as lack of energy, pain, bone-pain, shortness of breath, fatigue, blood in urine, etc. Each item is scored on a 5-point scale (0=not at all to 4=very much). FKSI-DRS total score ranged from 0 (no symptoms) to 36 (most severe symptoms) with a higher score indicating greater presence of kidney cancer symptoms. The baseline is defined as the last FKSI-DRS assessment on or prior to first day of treatment. A negative change from baseline indicates improvement in kidney cancer symptom status. 999 indicates data was not available

End point type	Secondary
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End point timeframe:

Baseline, Day 1 of Cycle 2, 3, 4, 5, 6, 7, 9, 11, 13, 16 and every 3rd cycle thereafter until end of treatment, and end of treatment, assessed up to approximately 38 months. Cycle=28 days

End point values	Pazopanib- 2nd line	Pazopanib- 3rd line	All participants	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	47	15	62	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Cycle 2 Day 1	-1.3 (± 4.95)	-0.3 (± 4.31)	-1.0 (± 4.78)	
Cycle 3 Day 1	-0.5 (± 4.55)	1.7 (± 4.18)	-0.0 (± 4.51)	
Cycle 4 Day 1	-0.1 (± 2.97)	1.8 (± 4.22)	0.2 (± 3.24)	
Cycle 5 Day 1	0.1 (± 3.13)	2.0 (± 2.35)	0.4 (± 3.06)	
Cycle 6 Day 1	-0.3 (± 5.68)	2.7 (± 3.27)	0.3 (± 5.36)	
Cycle 7 Day 1	-0.1 (± 3.47)	2.5 (± 3.73)	0.4 (± 3.63)	
Cycle 9 Day 1	-0.1 (± 4.22)	999 (± 999)	-0.1 (± 4.22)	
Cycle 11 Day 1	0.7 (± 3.30)	0.0 (± 999)	0.6 (± 3.20)	
Cycle 13 Day 1	1.4 (± 2.12)	999 (± 999)	1.4 (± 2.12)	
Cycle 16 Day 1	0.6 (± 1.59)	999 (± 999)	0.6 (± 1.59)	

Cycle 19 Day 1	0.0 (± 2.76)	999 (± 999)	0.0 (± 2.76)	
Cycle 22 Day 1	-0.5 (± 3.27)	999 (± 999)	-0.5 (± 3.27)	
Cycle 25 Day 1	2.0 (± 2.31)	999 (± 999)	2.0 (± 2.31)	
Cycle 28 Day 1	999 (± 999)	999 (± 999)	999 (± 999)	
Cycle 31 Day 1	0.5 (± 0.71)	999 (± 999)	0.5 (± 0.71)	
Cycle 34 Day 1	1.0 (± 999)	999 (± 999)	1.0 (± 999)	
Cycle 37 Day 1	1.0 (± 999)	999 (± 999)	1 (± 999)	
End of Treatment	-0.6 (± 3.86)	-0.8 (± 6.00)	-0.6 (± 4.37)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in EuroQoL 5-level instrument Visual Analogue Scale (EQ-5L-5D VAS) score

End point title	Change from baseline in EuroQoL 5-level instrument Visual Analogue Scale (EQ-5L-5D VAS) score
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End point description:

EQ-5D-5L is a standardized participant completed questionnaire that measures health-related quality of life and translates that score into an index value or utility score. EQ-5D-5L consists of two components: a health state profile and an optional visual analogue scale (VAS). The EQ-5L-5D VAS records the respondent's self-rated health on a vertical VAS, ranging from 0 (worst imaginable health state) to 100 (best imaginable health state), with higher scores indicating higher health-related quality of life.

The baseline is defined as the last EQ-5L-5D assessment on or prior to first day of treatment.

A positive change from baseline indicates improvement in the health state.

999 indicates data was not available

End point type	Secondary
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End point timeframe:

Baseline, Day 1 of Cycle 2, 3, 4, 5, 6, 7, 9, 11, 13, 16 and every 3rd cycle thereafter until end of treatment, and end of treatment, assessed up to approximately 38 months. Cycle=28 days

End point values	Pazopanib- 2nd line	Pazopanib- 3rd line	All participants	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	47	15	62	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Cycle 2 Day 1	0.1 (± 16.44)	-1.9 (± 19.46)	-0.4 (± 17.02)	
Cycle 3 Day 1	-2.8 (± 14.35)	3.6 (± 19.28)	-1.3 (± 15.58)	
Cycle 4 Day 1	-0.7 (± 10.88)	-1.5 (± 22.86)	-0.8 (± 13.27)	
Cycle 5 Day 1	-1.5 (± 13.61)	3.2 (± 19.51)	-0.7 (± 14.45)	
Cycle 6 Day 1	-1.3 (± 18.35)	-3.5 (± 24.09)	-1.7 (± 19.21)	
Cycle 7 Day 1	0.2 (± 11.89)	0.7 (± 20.37)	0.3 (± 13.73)	
Cycle 9 Day 1	3.8 (± 11.64)	999 (± 999)	3.8 (± 11.64)	
Cycle 11 Day 1	3.9 (± 12.62)	-2.0 (± 999)	3.5 (± 12.30)	
Cycle 13 Day 1	5.7 (± 12.26)	999 (± 999)	5.7 (± 12.26)	
Cycle 16 Day 1	-1.3 (± 11.70)	999 (± 999)	-1.3 (± 11.70)	
Cycle 19 Day 1	5.5 (± 10.09)	999 (± 999)	5.5 (± 10.09)	
Cycle 22 Day 1	0.5 (± 9.93)	999 (± 999)	0.5 (± 9.93)	

Cycle 25 Day 1	0.0 (± 9.70)	999 (± 999)	0.0 (± 9.70)	
Cycle 28 Day 1	999 (± 999)	999 (± 999)	999 (± 999)	
Cycle 31 Day 1	99.5 (± 0.71)	999 (± 999)	99.5 (± 0.71)	
Cycle 34 Day 1	10.0 (± 999)	999 (± 999)	10.0 (± 999)	
Cycle 37 Day 1	90.0 (± 999)	999 (± 999)	90.0 (± 999)	
End of Treatment	-1.9 (± 20.84)	-8.9 (± 19.99)	-3.6 (± 20.59)	

Statistical analyses

No statistical analyses for this end point

Post-hoc: All collected deaths

End point title	All collected deaths
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End point description:

On-treatment deaths were collected from first dose of study medication to 30 days after the last dose of study medication, for a maximum duration of approximately 38 months.

Post-treatment deaths were collected from day 31 after last dose of study medication to end of study, up to approximately 44 months.

All deaths refer to the sum of on-treatment deaths and post-treatment deaths.

End point type	Post-hoc
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End point timeframe:

On-treatment deaths: Up to approximately 38 months. Post-treatment deaths: Up to approximately 44 months

End point values	Pazopanib- 2nd line	Pazopanib- 3rd line	All participants	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	47	15	62	
Units: Participants				
On-treatment deaths	5	1	6	
Post-treatment deaths	22	10	32	
All deaths	27	11	38	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from first dose of study treatment until end of study treatment plus 30 days, up to a maximum duration of approximately 38 months

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.0
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Reporting groups

Reporting group title	Pazopanib- 2nd line
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Reporting group description:

Participants received pazopanib as 2nd line treatment

Reporting group title	All participants
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Reporting group description:

All participants who received pazopanib as 2nd or 3rd line treatment

Reporting group title	Pazopanib- 3rd line
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Reporting group description:

Participants received pazopanib as 3rd line treatment

Serious adverse events	Pazopanib- 2nd line	All participants	Pazopanib- 3rd line
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 47 (44.68%)	30 / 62 (48.39%)	9 / 15 (60.00%)
number of deaths (all causes)	5	6	1
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 47 (0.00%)	1 / 62 (1.61%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vasculitis			
subjects affected / exposed	1 / 47 (2.13%)	1 / 62 (1.61%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			

subjects affected / exposed	1 / 47 (2.13%)	1 / 62 (1.61%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	2 / 47 (4.26%)	2 / 62 (3.23%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Immune system disorder			
subjects affected / exposed	0 / 47 (0.00%)	1 / 62 (1.61%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	1 / 47 (2.13%)	2 / 62 (3.23%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	1 / 2	1 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrothorax			
subjects affected / exposed	0 / 47 (0.00%)	1 / 62 (1.61%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 47 (0.00%)	1 / 62 (1.61%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 47 (4.26%)	5 / 62 (8.06%)	3 / 15 (20.00%)
occurrences causally related to treatment / all	2 / 2	5 / 5	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	1 / 47 (2.13%)	1 / 62 (1.61%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Transaminases increased			
subjects affected / exposed	1 / 47 (2.13%)	2 / 62 (3.23%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	1 / 1	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	1 / 47 (2.13%)	1 / 62 (1.61%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			
subjects affected / exposed	1 / 47 (2.13%)	1 / 62 (1.61%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound haemorrhage			
subjects affected / exposed	1 / 47 (2.13%)	1 / 62 (1.61%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	1 / 47 (2.13%)	1 / 62 (1.61%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 47 (0.00%)	1 / 62 (1.61%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	1 / 47 (2.13%)	1 / 62 (1.61%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			

subjects affected / exposed	1 / 47 (2.13%)	1 / 62 (1.61%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 47 (0.00%)	1 / 62 (1.61%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 47 (0.00%)	1 / 62 (1.61%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 47 (0.00%)	1 / 62 (1.61%)	1 / 15 (6.67%)
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 / 47 (2.13%)	1 / 62 (1.61%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 47 (0.00%)	1 / 62 (1.61%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	0 / 47 (0.00%)	1 / 62 (1.61%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
subjects affected / exposed	3 / 47 (6.38%)	3 / 62 (4.84%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	3 / 3	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Skin and subcutaneous tissue disorders			
Pemphigoid			
subjects affected / exposed	1 / 47 (2.13%)	1 / 62 (1.61%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 47 (2.13%)	2 / 62 (3.23%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 1	1 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 47 (2.13%)	1 / 62 (1.61%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 47 (2.13%)	1 / 62 (1.61%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	2 / 47 (4.26%)	2 / 62 (3.23%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis viral			
subjects affected / exposed	0 / 47 (0.00%)	1 / 62 (1.61%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis bacterial			
subjects affected / exposed	1 / 47 (2.13%)	1 / 62 (1.61%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary sepsis			

subjects affected / exposed	1 / 47 (2.13%)	1 / 62 (1.61%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 47 (2.13%)	2 / 62 (3.23%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	1 / 47 (2.13%)	1 / 62 (1.61%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Pazopanib- 2nd line	All participants	Pazopanib- 3rd line
Total subjects affected by non-serious adverse events			
subjects affected / exposed	46 / 47 (97.87%)	60 / 62 (96.77%)	14 / 15 (93.33%)
Vascular disorders			
Hypertension			
subjects affected / exposed	13 / 47 (27.66%)	16 / 62 (25.81%)	3 / 15 (20.00%)
occurrences (all)	13	16	3
Hypotension			
subjects affected / exposed	0 / 47 (0.00%)	1 / 62 (1.61%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	6 / 47 (12.77%)	6 / 62 (9.68%)	0 / 15 (0.00%)
occurrences (all)	7	7	0
Fatigue			
subjects affected / exposed	15 / 47 (31.91%)	23 / 62 (37.10%)	8 / 15 (53.33%)
occurrences (all)	19	32	13
Gait disturbance			
subjects affected / exposed	0 / 47 (0.00%)	1 / 62 (1.61%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Oedema peripheral			

subjects affected / exposed occurrences (all)	3 / 47 (6.38%) 4	4 / 62 (6.45%) 7	1 / 15 (6.67%) 3
Pain			
subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	1 / 62 (1.61%) 1	1 / 15 (6.67%) 1
Pyrexia			
subjects affected / exposed occurrences (all)	3 / 47 (6.38%) 3	4 / 62 (6.45%) 4	1 / 15 (6.67%) 1
Peripheral swelling			
subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	2 / 62 (3.23%) 2	1 / 15 (6.67%) 1
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	1 / 62 (1.61%) 1	1 / 15 (6.67%) 1
Dysphonia			
subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	2 / 62 (3.23%) 2	1 / 15 (6.67%) 1
Cough			
subjects affected / exposed occurrences (all)	4 / 47 (8.51%) 4	6 / 62 (9.68%) 6	2 / 15 (13.33%) 2
Dyspnoea			
subjects affected / exposed occurrences (all)	2 / 47 (4.26%) 2	4 / 62 (6.45%) 4	2 / 15 (13.33%) 2
Epistaxis			
subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	2 / 62 (3.23%) 2	2 / 15 (13.33%) 2
Haemoptysis			
subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	2 / 62 (3.23%) 2	1 / 15 (6.67%) 1
Pharyngeal erythema			
subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	1 / 62 (1.61%) 1	1 / 15 (6.67%) 1
Sinus congestion			

subjects affected / exposed	0 / 47 (0.00%)	1 / 62 (1.61%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Pulmonary embolism			
subjects affected / exposed	0 / 47 (0.00%)	1 / 62 (1.61%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 47 (2.13%)	2 / 62 (3.23%)	1 / 15 (6.67%)
occurrences (all)	1	2	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	7 / 47 (14.89%)	12 / 62 (19.35%)	5 / 15 (33.33%)
occurrences (all)	7	12	5
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 47 (10.64%)	9 / 62 (14.52%)	4 / 15 (26.67%)
occurrences (all)	5	10	5
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 47 (4.26%)	6 / 62 (9.68%)	4 / 15 (26.67%)
occurrences (all)	2	6	4
Blood bilirubin increased			
subjects affected / exposed	3 / 47 (6.38%)	7 / 62 (11.29%)	4 / 15 (26.67%)
occurrences (all)	3	8	5
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 47 (0.00%)	1 / 62 (1.61%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Blood creatinine increased			
subjects affected / exposed	3 / 47 (6.38%)	4 / 62 (6.45%)	1 / 15 (6.67%)
occurrences (all)	3	4	1
Blood glucose increased			
subjects affected / exposed	0 / 47 (0.00%)	1 / 62 (1.61%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Blood urea increased			
subjects affected / exposed	0 / 47 (0.00%)	1 / 62 (1.61%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Gamma-glutamyltransferase increased			

subjects affected / exposed	1 / 47 (2.13%)	4 / 62 (6.45%)	3 / 15 (20.00%)
occurrences (all)	1	4	3
Lipase increased			
subjects affected / exposed	3 / 47 (6.38%)	3 / 62 (4.84%)	0 / 15 (0.00%)
occurrences (all)	3	3	0
Platelet count decreased			
subjects affected / exposed	0 / 47 (0.00%)	1 / 62 (1.61%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Serum ferritin increased			
subjects affected / exposed	0 / 47 (0.00%)	1 / 62 (1.61%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Transaminases increased			
subjects affected / exposed	2 / 47 (4.26%)	3 / 62 (4.84%)	1 / 15 (6.67%)
occurrences (all)	2	3	1
Troponin T increased			
subjects affected / exposed	0 / 47 (0.00%)	1 / 62 (1.61%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Weight decreased			
subjects affected / exposed	8 / 47 (17.02%)	10 / 62 (16.13%)	2 / 15 (13.33%)
occurrences (all)	8	12	4
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 47 (0.00%)	1 / 62 (1.61%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 47 (2.13%)	2 / 62 (3.23%)	1 / 15 (6.67%)
occurrences (all)	1	2	1
Dysgeusia			
subjects affected / exposed	5 / 47 (10.64%)	10 / 62 (16.13%)	5 / 15 (33.33%)
occurrences (all)	7	13	6
Headache			
subjects affected / exposed	1 / 47 (2.13%)	3 / 62 (4.84%)	2 / 15 (13.33%)
occurrences (all)	1	3	2
Lethargy			

subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	1 / 62 (1.61%) 1	1 / 15 (6.67%) 1
Blood and lymphatic system disorders Thrombocytopenia subjects affected / exposed occurrences (all)	3 / 47 (6.38%) 3	4 / 62 (6.45%) 4	1 / 15 (6.67%) 1
Anaemia subjects affected / exposed occurrences (all)	3 / 47 (6.38%) 3	4 / 62 (6.45%) 4	1 / 15 (6.67%) 1
Eye disorders Lacrimation increased subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	1 / 62 (1.61%) 1	1 / 15 (6.67%) 1
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	5 / 47 (10.64%) 7	7 / 62 (11.29%) 11	2 / 15 (13.33%) 4
Abdominal pain upper subjects affected / exposed occurrences (all)	5 / 47 (10.64%) 5	5 / 62 (8.06%) 5	0 / 15 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	24 / 47 (51.06%) 32	30 / 62 (48.39%) 39	6 / 15 (40.00%) 7
Constipation subjects affected / exposed occurrences (all)	5 / 47 (10.64%) 5	7 / 62 (11.29%) 7	2 / 15 (13.33%) 2
Enterocolitis subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	1 / 62 (1.61%) 1	1 / 15 (6.67%) 1
Gastritis subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	2 / 62 (3.23%) 2	1 / 15 (6.67%) 1
Gastrointestinal pain subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	1 / 62 (1.61%) 3	1 / 15 (6.67%) 3
Haemorrhoids			

subjects affected / exposed	1 / 47 (2.13%)	2 / 62 (3.23%)	1 / 15 (6.67%)
occurrences (all)	1	2	1
Nausea			
subjects affected / exposed	12 / 47 (25.53%)	16 / 62 (25.81%)	4 / 15 (26.67%)
occurrences (all)	13	19	6
Rectal haemorrhage			
subjects affected / exposed	1 / 47 (2.13%)	2 / 62 (3.23%)	1 / 15 (6.67%)
occurrences (all)	1	2	1
Stomatitis			
subjects affected / exposed	6 / 47 (12.77%)	8 / 62 (12.90%)	2 / 15 (13.33%)
occurrences (all)	7	9	2
Vomiting			
subjects affected / exposed	6 / 47 (12.77%)	9 / 62 (14.52%)	3 / 15 (20.00%)
occurrences (all)	6	9	3
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	4 / 47 (8.51%)	4 / 62 (6.45%)	0 / 15 (0.00%)
occurrences (all)	4	4	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 47 (2.13%)	2 / 62 (3.23%)	1 / 15 (6.67%)
occurrences (all)	1	2	1
Dry skin			
subjects affected / exposed	0 / 47 (0.00%)	1 / 62 (1.61%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Erythema			
subjects affected / exposed	2 / 47 (4.26%)	3 / 62 (4.84%)	1 / 15 (6.67%)
occurrences (all)	2	3	1
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	5 / 47 (10.64%)	8 / 62 (12.90%)	3 / 15 (20.00%)
occurrences (all)	5	10	5
Pruritus			
subjects affected / exposed	3 / 47 (6.38%)	3 / 62 (4.84%)	0 / 15 (0.00%)
occurrences (all)	3	3	0
Rash			

subjects affected / exposed occurrences (all)	3 / 47 (6.38%) 3	4 / 62 (6.45%) 4	1 / 15 (6.67%) 1
Rash macular subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	1 / 62 (1.61%) 1	1 / 15 (6.67%) 1
Rash maculo-papular subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	1 / 62 (1.61%) 1	1 / 15 (6.67%) 1
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	1 / 62 (1.61%) 1	1 / 15 (6.67%) 1
Proteinuria subjects affected / exposed occurrences (all)	3 / 47 (6.38%) 4	5 / 62 (8.06%) 6	2 / 15 (13.33%) 2
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	3 / 47 (6.38%) 3	6 / 62 (9.68%) 6	3 / 15 (20.00%) 3
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	4 / 47 (8.51%) 4	4 / 62 (6.45%) 4	0 / 15 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	5 / 47 (10.64%) 5	5 / 62 (8.06%) 5	0 / 15 (0.00%) 0
Flank pain subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	1 / 62 (1.61%) 1	1 / 15 (6.67%) 1
Joint swelling subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	1 / 62 (1.61%) 1	1 / 15 (6.67%) 1
Muscle spasms subjects affected / exposed occurrences (all)	3 / 47 (6.38%) 3	4 / 62 (6.45%) 4	1 / 15 (6.67%) 1
Pain in extremity			

subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	2 / 62 (3.23%) 3	1 / 15 (6.67%) 2
Infections and infestations			
Lower respiratory tract infection subjects affected / exposed occurrences (all)	2 / 47 (4.26%) 2	3 / 62 (4.84%) 4	1 / 15 (6.67%) 2
Nasopharyngitis subjects affected / exposed occurrences (all)	2 / 47 (4.26%) 2	3 / 62 (4.84%) 3	1 / 15 (6.67%) 1
Rhinitis subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	1 / 62 (1.61%) 1	1 / 15 (6.67%) 1
Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	2 / 62 (3.23%) 2	1 / 15 (6.67%) 1
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	14 / 47 (29.79%) 16	17 / 62 (27.42%) 20	3 / 15 (20.00%) 4
Hyperglycaemia subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 2	2 / 62 (3.23%) 3	1 / 15 (6.67%) 1
Hyponatraemia subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	2 / 62 (3.23%) 2	2 / 15 (13.33%) 2
Iron deficiency subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	1 / 62 (1.61%) 1	1 / 15 (6.67%) 1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 February 2018	<p>The sample size was reduced from 140 to approximately 100 subjects, considering the potential challenges in the recruitment with the availability of other treatment options in the RCC landscape.</p> <p>The number of prior lines of therapy was captured in the IRT system at screening, with an enrolment cap of 60 subjects receiving pazopanib in 3L, to ensure that at least 40 subjects would be in the 2L treatment subgroup.</p> <p>As there was limited evidence to support re-challenge with pazopanib after prior 1st line pazopanib followed by ICI, the exclusion criteria were modified to exclude subjects with previous exposure to pazopanib.</p> <p>To allow for early monitoring of blood pressure soon after starting treatment with pazopanib, vital signs measurement was added on Cycle 1 Day 8. The frequency of cardiac imaging was reduced to every 5-6 cycles unless otherwise indicated.</p>
14 September 2020	<p>Novartis procedures for collecting follow up information on pregnancies were revised to harmonize follow-up timelines across product platforms. The follow up period for collecting information after a live birth has been extended from 3 months to 12 months.</p>

Notes:

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.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use <https://www.novctrd.com> for complete trial results.

Notes: