NOVARTIS

Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Pazopanib

Trial Indication(s)

Advanced and/or metastatic renal cell carcinoma

Protocol Number

CPZP034A2410

Protocol Title

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

Clinical Trial Phase

Phase 2

Phase of Drug Development

Phase IV

Study Start/End Dates

Study Start Date: November 2017 (Actual)
Primary Completion Date: August 2021 (Actual)
Study Completion Date: August 2021 (Actual)

Reason for Termination (If applicable)

Not applicable

Study Design/Methodology

This was a multi-center, open-label, single-arm Phase II study to determine the efficacy, tolerability, safety and quality of life of treatment with pazopanib in subjects with advanced and/or metastatic renal cell carcinoma (RCC) following prior treatment with immune checkpoint inhibitors (ICI).

Subjects could have received prior systemic therapy with an ICI (monotherapy or combination) as 1st or 2nd line RCC treatment. However, they must not have received pazopanib previously. In this study, pazopanib could be administered in the 2nd or 3rd line setting. The therapeutic line for individual subjects was assigned at the time of screening.

Subjects received 800 mg of pazopanib daily until disease progression, unacceptable toxicity, death, pregnancy, start of a new anti-neoplastic therapy, discontinuation at the discretion of the investigator or patient, lost to follow-up or end of study, whichever came first.

After discontinuation of study treatment:

- Safety follow-up: all subjects were followed for safety up to 30 days except in case of death, loss to follow up or withdrawal of consent.
- Efficacy follow-up: Subjects who discontinued study treatment without disease progression (by RECIST 1.1) before end of recruitment period date + 1 year were continued to be followed for efficacy until disease progression, death, pregnancy, withdrawal of consent, loss to follow-up, subject/guardian decision, study terminated by sponsor or until end of recruitment period date + 1 year, whichever came first (efficacy follow-up period).
- Survival follow-up: Subjects were followed for survival until end of recruitment period date + 2 years. Subjects who discontinued study treatment without documented disease progression and entered the efficacy follow-up were not allowed to begin survival follow-up until after the efficacy follow-up period.

Centers

22 centers in 11 countries: Czech Republic(2), Hungary(1), Austria(3), United Kingdom(3), Spain(2), Germany(3), Chile(2), Argentina(1), Canada(1), United States(1), France(3)

Objectives:

Primary Objective:

- To assess the progression-free survival (PFS) based on local investigator assessment.

Secondary Objectives:

- To assess overall response rate (ORR) and clinical benefit rate (CBR) based on local investigator assessment.
- To assess overall survival (OS)
- To assess duration of response (DOR) in subjects with complete response or partial response
- To evaluate the safety and tolerability
- To assess quality of life

Test Product (s), Dose(s), and Mode(s) of Administration

Pazopanib (aqueous film-coated tablets) was administered as a fixed oral dose of 800 mg daily in treatment cycles of 28 days (4 weeks) each.

Statistical Methods

The primary endpoint of the study is PFS, defined as the time from the date of start of study treatment to the date of the first documented progression or death due to any cause. For the primary efficacy analysis, PFS was based on local Investigator's review of tumor assessments using RECIST v1.1 criteria. If a subject had not progressed or died at the analysis cut-off date, PFS was censored at the date of the last adequate tumor evaluation date before the cut-off date. The PFS distribution was estimated using the Kaplan-Meier method.

The key secondary endpoint, OS is defined as the time from date of start of treatment to date of 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.

ORR is defined as the proportion of subjects with best overall response (BOR) of complete response (CR) or partial response (PR) according to RECIST 1.1. ORR was calculated using local Investigators review of tumor assessment data.

CBR is defined as the proportion of subjects with a best overall response (BOR) of confirmed CR or PR, or SD or Non-CR/Non-PD lasting 24 weeks or longer, according to RECIST v1.1 criteria. CBR was calculated based on the Investigators' tumor assessments.

DOR only applies to subjects whose best overall response was CR or PR according to RECIST v1.1 based on local Investigators review of tumor assessment data. DOR was computed from the first documented response of CR or PR till the first documented progression or death due to underlying cancer. Subjects continuing without progression or death due to underlying cancer were censored at the date of their last adequate tumor assessment. The DOR distribution was calculated using the Kaplan-Meier method.

The quality of life was assessed by change from baseline in the Functional Assessment of Cancer Therapy- Kidney Symptom (FKSI-DRS) and EuroQoL 5-level (EQ-5D-5L) scores. The baseline was defined as the last assessment on or prior to first day of treatment.

Study Population: Key Inclusion/Exclusion Criteria

Key Inclusion Criteria:

- Histologically confirmed locally recurrent or metastatic predominantly clear cell renal cell carcinoma.
- Measurable disease based on RECIST 1.1 criteria
- Prior systemic therapy with an immune checkpoint inhibitor (monotherapy or combination) as 1st or 2nd line RCC treatment. Note: patients with prior mTOR inhibitor or TKI treatment as monotherapy or in combination with immune checkpoint inhibitor were allowed; however, treatment with immune checkpoint inhibitor (monotherapy or in combination) must have been the last treatment prior to study entry.
- Last dose of immune checkpoint inhibitor therapy received 4 or more weeks before start of study treatment
- Karnofsky performance status ≥70%.
- Potassium, sodium, calcium and magnesium within normal limits of the central laboratory

Key Exclusion Criteria:

- Renal cell carcinoma without any clear (conventional) cell component
- History or evidence of central nervous system (CNS) metastases (patients with pretreated metastases were eligible under certain conditions)
- Prior treatment with pazopanib
- Prior treatment with bevacizumab that was not given in combination with immune checkpoint inhibitor therapy.
- Prior treatment with more than 2 lines of therapy (combination treatments were considered 1 line of therapy)
- Not recovered from toxicity from prior immune checkpoint inhibitor therapy. Recovery was defined as ≤ NCI-CTCAE Grade 1,

except for liver function test levels which must be <Grade 1.
• Disease recurrence less than 6 months from the last dose of prior neoadjuvant or adjuvant therapy (including VEGF-R TKI)
• Patients receiving prohibited concomitant medications that could not be discontinued or replaced by safe alternative medication at least 5 half-lives of the concomitant medication or 7 days, whichever was longer, prior to the start of pazopanib treatment.
• Administration of any investigational drug within 4 weeks prior to the first dose of study treatment

Participant Flow Table

Overall Study

	Pazopanib-2nd line	Pazopanib-3rd line	Total
Arm/Group Description	Participants received pazopanib as 2nd line treatment	Participants received pazopanib as 3rd line treatment	
Started	47	15	62
Completed	6	0	6
Not Completed	41	15	56
Progressive disease	24	5	29
Adverse Event	11	8	19
Physician Decision	3	2	5
Death	2	0	2
Subject/Guardian Decision	1	0	1

Baseline Characteristics

	Pazopanib-2nd line	Pazopanib-3rd line	Total
Arm/Group Description	Participants received pazopanib as 2nd line treatment	Participants received pazopanib as 3rd line treatment	
Number of Participants [units: participants]	47	15	62
Age Continuous (units: Years) Mean ± Standard Deviation			
	62.4±11.55	65.4±9.77	63.2±11.15
Sex: Female, Male (units: Participants) Count of Participants (Not Applicable)			
Female	11	4	15
Male	36	11	47
Race/Ethnicity, Customized (units: Participants) Count of Participants (Not Applicable)			
White	44	13	57
Asian	1	0	1
Other	0	1	1
Unknown	2	1	3

Primary Outcome Result(s)

Progression free survival (PFS)

(Time Frame: Date of first treatment to date of progression or death up to approximately 38 months)

	Pazopanib-2nd line	Pazopanib-3rd line	All participants
Arm/Group Description	Participants received pazopanib as 2nd line treatment	Participants received pazopanib as 3rd line treatment	All participants who received pazopanib as 2nd or 3rd line treatment
Number of Participants Analyzed [units: participants]	47	15	62
Progression free survival (PFS) (units: Months) Median (95% Confidence Interval)			
	7.5 (3.7 to 12.6)	4.6 (3.3 to 9.2)	6.8 (3.7 to 11.1)

Secondary Outcome Result(s)

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

(Time Frame: Up to approximately 38 months)

	Pazopanib-2nd line	Pazopanib-3rd line	All participants
Arm/Group Description	Participants received pazopanib as	Participants received pazopanib as	All participants who received pazopanib as

	2nd line treatment	3rd line treatment	2nd or 3rd line treatment
Number of Participants Analyzed [units: participants]	47	15	62
Overall response rate (ORR) based on local investigator assessment according to RECIST v1.1 (units: Percentage of participants) Number (95% Confidence Interval)			
	23.4 (12.3 to 38.0)	0 (0.0 to 21.8)	17.7 (9.2 to 29.5)

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

(Time Frame: Up to approximately 38 months)

	Pazopanib-2nd line	**Pazopanib-3rd line**	**All participants**
Arm/Group Description	Participants received pazopanib as 2nd line treatment	Participants received pazopanib as 3rd line treatment	All participants who received pazopanib as 2nd or 3rd line treatment
Number of Participants Analyzed [units: participants]	47	15	62
Clinical benefit rate (CBR) based on local investigator assessment according to RECIST v1.1. (units: Percentage of			

participants) Number (95% Confidence Interval)			
	53.2 (38.1 to 67.9)	40.0 (16.3 to 67.7)	50.0 (37.0 to 63.0)

Overall survival (OS)

(Time Frame: From date of first treatment to date of death, up to approximately 44 months)

	Pazopanib-2nd line	Pazopanib-3rd line	All participants
Arm/Group Description	Participants received pazopanib as 2nd line treatment	Participants received pazopanib as 3rd line treatment	All participants who received pazopanib as 2nd or 3rd line treatment
Number of Participants Analyzed [units: participants]	47	15	62
Overall survival (OS) (units: Months) Median (95% Confidence Interval)			
	27.8 (14.9 to NA)[1]	20.0 (9.2 to 25.6)	23.4 (14.9 to 31.8)

[1] NA: Not estimable due to insufficient follow-up time

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

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

	Pazopanib-2nd line	Pazopanib-3rd line
Arm/Group Description	Participants received pazopanib as	Participants received pazopanib as

	2nd line treatment	3rd line treatment
Number of Participants Analyzed [units: participants]	11	0
Duration of response (DOR) based on local Investigators assessment according to RECIST v1.1 (units: Months) Median (95% Confidence Interval)	NA (9.5 to NA)[1]	

[1] NA: Not estimable due to insufficient number of participants with events

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

(Time Frame: 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)

	Pazopanib-2nd line	**Pazopanib-3rd line**	**All participants**
Arm/Group Description	Participants received pazopanib as 2nd line treatment	Participants received pazopanib as 3rd line treatment	All participants who received pazopanib as 2nd or 3rd line treatment
Number of Participants Analyzed [units: participants]	47	15	62
Change from baseline in Functional Assessment of Cancer Therapy-Kidney Symptom (FKSI-DRS) score (units: Score on a scale) 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		-0.1 ± 4.22
Cycle 11 Day 1	0.7 ± 3.30	0.0 ± NA[1]	0.6 ± 3.20
Cycle 13 Day 1	1.4 ± 2.12		1.4 ± 2.12
Cycle 16 Day 1	0.6 ± 1.59		0.6 ± 1.59
Cycle 19 Day 1	0.0 ± 2.76		0.0 ± 2.76
Cycle 22 Day 1	-0.5 ± 3.27		-0.5 ± 3.27
Cycle 25 Day 1	2.0 ± 2.31		2.0 ± 2.31
Cycle 28 Day 1			
Cycle 31 Day 1	0.5 ± 0.71		0.5 ± 0.71
Cycle 34 Day 1	1.0 ± NA[2345]		1.0 ± NA[2345]
Cycle 37 Day 1	1.0 ± NA[2345]		1 ± NA[2345]
End of Treatment	-0.6 ± 3.86	-0.8 ± 6.00	-0.6 ± 4.37

[1] NA: The standard deviation was not estimable as there was only one participant.
[2] NA: The standard deviation was not estimable as there was only one participant
[3] NA: The standard deviation was not estimable as there was only one participant
[4] NA: The standard deviation was not estimable as there was only one participant
[5] NA: The standard deviation was not estimable as there was only one participant

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

(Time Frame: 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)

	Pazopanib-2nd line	Pazopanib-3rd line	All participants
Arm/Group Description	Participants received pazopanib as 2nd line treatment	Participants received pazopanib as 3rd line treatment	All participants who received pazopanib as 2nd or 3rd line treatment
Number of Participants Analyzed [units: participants]	47	15	62
Change from baseline in EuroQoL 5-level instrument Visual Analogue Scale (EQ-5L-5D VAS) score (units: Score on a scale) 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		3.8 ± 11.64
Cycle 11 Day 1	3.9 ± 12.62	-2.0 ± NA[12345]	3.5 ± 12.30
Cycle 13 Day 1	5.7 ± 12.26		5.7 ± 12.26
Cycle 16 Day 1	-1.3 ± 11.70		-1.3 ± 11.70
Cycle 19 Day 1	5.5 ± 10.09		5.5 ± 10.09
Cycle 22 Day 1	0.5 ± 9.93		0.5 ± 9.93
Cycle 25 Day 1	0.0 ± 9.70		0.0 ± 9.70
Cycle 28 Day 1			

Cycle 31 Day 1	99.5 ± 0.71		99.5 ± 0.71
Cycle 34 Day 1	10.0 ± NA[12345]		10.0 ± NA[12345]
Cycle 37 Day 1	90.0 ± NA[12345]		90.0 ± NA[12345]
End of Treatment	-1.9 ± 20.84	-8.9 ± 19.99	-3.6 ± 20.59

[1] NA: The standard deviation was not estimable as there was only one participant.
[2] NA: The standard deviation was not estimable as there was only one participant.
[3] NA: The standard deviation was not estimable as there was only one participant.
[4] NA: The standard deviation was not estimable as there was only one participant.
[5] NA: The standard deviation was not estimable as there was only one participant.

All collected deaths

(Time Frame: On-treatment deaths: Up to approximately 38 months. Post-treatment deaths: Up to approximately 44 months)

	Pazopanib-2nd line	**Pazopanib-3rd line**	**All participants**
Arm/Group Description	Participants received pazopanib as 2nd line treatment	Participants received pazopanib as 3rd line treatment	All participants who received pazopanib as 2nd or 3rd line treatment
Number of Participants Analyzed [units: participants]	47	15	62
All collected deaths (units: Participants) Count of Participants (Not Applicable)			
On-treatment deaths	5 (10.64%)	1 (6.67%)	6 (9.68%)
Post-treatment deaths	22 (46.81%)	10 (66.67%)	32 (51.61%)
All deaths	27 (57.45%)	11 (73.33%)	38 (61.29%)

Safety Results

All-Cause Mortality

	Pazopanib-2nd line N = 47	Pazopanib-3rd line N = 15	All participants N = 62
Arm/Group Description	Participants received pazopanib as 2nd line treatment	Participants received pazopanib as 3rd line treatment	All participants who received pazopanib as 2nd or 3rd line treatment
Total participants affected	5 (10.64%)	1 (6.67%)	6 (9.68%)

Serious Adverse Events by System Organ Class

Time Frame	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
Additional Description	Any sign or symptom that occurs during the study treatment plus the 30 days post treatment
Source Vocabulary for Table Default	MedDRA (24.0)
Assessment Type for Table Default	Systematic Assessment

	Pazopanib-2nd line N = 47	Pazopanib-3rd line N = 15	All participants N = 62
Arm/Group Description	Participants received pazopanib as 2nd line treatment	Participants received pazopanib as 3rd line treatment	All participants who received pazopanib as 2nd or 3rd line treatment
Total participants affected	21 (44.68%)	9 (60.00%)	30 (48.39%)
Blood and lymphatic system disorders			
Anaemia	0 (0.00%)	1 (6.67%)	1 (1.61%)
Cardiac disorders			
Atrial flutter	1 (2.13%)	0 (0.00%)	1 (1.61%)
Gastrointestinal disorders			
Abdominal pain upper	0 (0.00%)	1 (6.67%)	1 (1.61%)
Ascites	0 (0.00%)	1 (6.67%)	1 (1.61%)
Diarrhoea	1 (2.13%)	0 (0.00%)	1 (1.61%)
Vomiting	0 (0.00%)	1 (6.67%)	1 (1.61%)
General disorders and administration site conditions			
Chest pain	1 (2.13%)	0 (0.00%)	1 (1.61%)
Pyrexia	2 (4.26%)	0 (0.00%)	2 (3.23%)
Hepatobiliary disorders			
Drug-induced liver injury	0 (0.00%)	1 (6.67%)	1 (1.61%)

Hepatotoxicity	3 (6.38%)	0 (0.00%)	3 (4.84%)
Immune system disorders			
Immune system disorder	0 (0.00%)	1 (6.67%)	1 (1.61%)
Infections and infestations			
Bronchitis viral	0 (0.00%)	1 (6.67%)	1 (1.61%)
Meningitis bacterial	1 (2.13%)	0 (0.00%)	1 (1.61%)
Pulmonary sepsis	1 (2.13%)	0 (0.00%)	1 (1.61%)
Urinary tract infection	1 (2.13%)	1 (6.67%)	2 (3.23%)
Viral infection	1 (2.13%)	0 (0.00%)	1 (1.61%)
Injury, poisoning and procedural complications			
Hip fracture	1 (2.13%)	0 (0.00%)	1 (1.61%)
Spinal fracture	1 (2.13%)	0 (0.00%)	1 (1.61%)
Wound haemorrhage	1 (2.13%)	0 (0.00%)	1 (1.61%)
Investigations			
Alanine aminotransferase increased	2 (4.26%)	3 (20.00%)	5 (8.06%)
Blood bilirubin increased	1 (2.13%)	0 (0.00%)	1 (1.61%)
Transaminases increased	1 (2.13%)	1 (6.67%)	2 (3.23%)
Musculoskeletal and connective tissue disorders			
Arthralgia	1 (2.13%)	0 (0.00%)	1 (1.61%)

Back pain	2 (4.26%)	0 (0.00%)	2 (3.23%)
Nervous system disorders			
Cerebrovascular accident	0 (0.00%)	1 (6.67%)	1 (1.61%)
Dizziness	1 (2.13%)	0 (0.00%)	1 (1.61%)
Spinal cord compression	1 (2.13%)	0 (0.00%)	1 (1.61%)
Renal and urinary disorders			
Acute kidney injury	1 (2.13%)	1 (6.67%)	2 (3.23%)
Renal failure	1 (2.13%)	0 (0.00%)	1 (1.61%)
Respiratory, thoracic and mediastinal disorders			
Haemoptysis	1 (2.13%)	1 (6.67%)	2 (3.23%)
Hydrothorax	0 (0.00%)	1 (6.67%)	1 (1.61%)
Pleural effusion	0 (0.00%)	1 (6.67%)	1 (1.61%)
Skin and subcutaneous tissue disorders			
Pemphigoid	1 (2.13%)	0 (0.00%)	1 (1.61%)
Vascular disorders			
Hypertension	0 (0.00%)	1 (6.67%)	1 (1.61%)
Vasculitis	1 (2.13%)	0 (0.00%)	1 (1.61%)

Other Adverse Events by System Organ Class

Time Frame	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
Additional Description	Any sign or symptom that occurs during the study treatment plus the 30 days post treatment
Source Vocabulary for Table Default	MedDRA (24.0)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	5%

	Pazopanib-2nd line N = 47	**Pazopanib-3rd line N = 15**	**All participants N = 62**
Arm/Group Description	Participants received pazopanib as 2nd line treatment	Participants received pazopanib as 3rd line treatment	All participants who received pazopanib as 2nd or 3rd line treatment
Total participants affected	46 (97.87%)	14 (93.33%)	60 (96.77%)
Blood and lymphatic system disorders			
Anaemia	3 (6.38%)	1 (6.67%)	4 (6.45%)
Thrombocytopenia	3 (6.38%)	1 (6.67%)	4 (6.45%)
Endocrine disorders			
Hypothyroidism	3 (6.38%)	3 (20.00%)	6 (9.68%)
Eye disorders			
Lacrimation increased	0 (0.00%)	1 (6.67%)	1 (1.61%)
Gastrointestinal disorders			

Abdominal pain	5 (10.64%)	2 (13.33%)	7 (11.29%)
Abdominal pain upper	5 (10.64%)	0 (0.00%)	5 (8.06%)
Constipation	5 (10.64%)	2 (13.33%)	7 (11.29%)
Diarrhoea	24 (51.06%)	6 (40.00%)	30 (48.39%)
Enterocolitis	0 (0.00%)	1 (6.67%)	1 (1.61%)
Gastritis	1 (2.13%)	1 (6.67%)	2 (3.23%)
Gastrointestinal pain	0 (0.00%)	1 (6.67%)	1 (1.61%)
Haemorrhoids	1 (2.13%)	1 (6.67%)	2 (3.23%)
Nausea	12 (25.53%)	4 (26.67%)	16 (25.81%)
Rectal haemorrhage	1 (2.13%)	1 (6.67%)	2 (3.23%)
Stomatitis	6 (12.77%)	2 (13.33%)	8 (12.90%)
Vomiting	6 (12.77%)	3 (20.00%)	9 (14.52%)
General disorders and administration site conditions			
Asthenia	6 (12.77%)	0 (0.00%)	6 (9.68%)
Fatigue	15 (31.91%)	8 (53.33%)	23 (37.10%)
Gait disturbance	0 (0.00%)	1 (6.67%)	1 (1.61%)
Oedema peripheral	3 (6.38%)	1 (6.67%)	4 (6.45%)
Pain	0 (0.00%)	1 (6.67%)	1 (1.61%)
Peripheral swelling	1 (2.13%)	1 (6.67%)	2 (3.23%)
Pyrexia	3 (6.38%)	1 (6.67%)	4 (6.45%)
Hepatobiliary disorders			
Hepatotoxicity	4 (8.51%)	0 (0.00%)	4 (6.45%)
Infections and infestations			

Lower respiratory tract infection	2 (4.26%)	1 (6.67%)	3 (4.84%)
Nasopharyngitis	2 (4.26%)	1 (6.67%)	3 (4.84%)
Rhinitis	0 (0.00%)	1 (6.67%)	1 (1.61%)
Upper respiratory tract infection	1 (2.13%)	1 (6.67%)	2 (3.23%)
Injury, poisoning and procedural complications			
Fall	0 (0.00%)	1 (6.67%)	1 (1.61%)
Investigations			
Alanine aminotransferase increased	7 (14.89%)	5 (33.33%)	12 (19.35%)
Aspartate aminotransferase increased	5 (10.64%)	4 (26.67%)	9 (14.52%)
Blood alkaline phosphatase increased	2 (4.26%)	4 (26.67%)	6 (9.68%)
Blood bilirubin increased	3 (6.38%)	4 (26.67%)	7 (11.29%)
Blood creatine phosphokinase increased	0 (0.00%)	1 (6.67%)	1 (1.61%)
Blood creatinine increased	3 (6.38%)	1 (6.67%)	4 (6.45%)
Blood glucose increased	0 (0.00%)	1 (6.67%)	1 (1.61%)
Blood urea increased	0 (0.00%)	1 (6.67%)	1 (1.61%)
Gamma-glutamyltransferase increased	1 (2.13%)	3 (20.00%)	4 (6.45%)

Lipase increased	3 (6.38%)	0 (0.00%)	3 (4.84%)
Platelet count decreased	0 (0.00%)	1 (6.67%)	1 (1.61%)
Serum ferritin increased	0 (0.00%)	1 (6.67%)	1 (1.61%)
Transaminases increased	2 (4.26%)	1 (6.67%)	3 (4.84%)
Troponin T increased	0 (0.00%)	1 (6.67%)	1 (1.61%)
Weight decreased	8 (17.02%)	2 (13.33%)	10 (16.13%)
Metabolism and nutrition disorders			
Decreased appetite	14 (29.79%)	3 (20.00%)	17 (27.42%)
Hyperglycaemia	1 (2.13%)	1 (6.67%)	2 (3.23%)
Hyponatraemia	0 (0.00%)	2 (13.33%)	2 (3.23%)
Iron deficiency	0 (0.00%)	1 (6.67%)	1 (1.61%)
Musculoskeletal and connective tissue disorders			
Arthralgia	4 (8.51%)	0 (0.00%)	4 (6.45%)
Back pain	5 (10.64%)	0 (0.00%)	5 (8.06%)
Flank pain	0 (0.00%)	1 (6.67%)	1 (1.61%)
Joint swelling	0 (0.00%)	1 (6.67%)	1 (1.61%)
Muscle spasms	3 (6.38%)	1 (6.67%)	4 (6.45%)
Pain in extremity	1 (2.13%)	1 (6.67%)	2 (3.23%)
Nervous system disorders			
Dizziness	1 (2.13%)	1 (6.67%)	2 (3.23%)
Dysgeusia	5 (10.64%)	5 (33.33%)	10 (16.13%)
Headache	1 (2.13%)	2 (13.33%)	3 (4.84%)

Lethargy	0 (0.00%)	1 (6.67%)	1 (1.61%)
Psychiatric disorders			
Depression	1 (2.13%)	1 (6.67%)	2 (3.23%)
Renal and urinary disorders			
Dysuria	0 (0.00%)	1 (6.67%)	1 (1.61%)
Proteinuria	3 (6.38%)	2 (13.33%)	5 (8.06%)
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease	0 (0.00%)	1 (6.67%)	1 (1.61%)
Cough	4 (8.51%)	2 (13.33%)	6 (9.68%)
Dysphonia	1 (2.13%)	1 (6.67%)	2 (3.23%)
Dyspnoea	2 (4.26%)	2 (13.33%)	4 (6.45%)
Epistaxis	0 (0.00%)	2 (13.33%)	2 (3.23%)
Haemoptysis	1 (2.13%)	1 (6.67%)	2 (3.23%)
Pharyngeal erythema	0 (0.00%)	1 (6.67%)	1 (1.61%)
Pulmonary embolism	0 (0.00%)	1 (6.67%)	1 (1.61%)
Sinus congestion	0 (0.00%)	1 (6.67%)	1 (1.61%)
Skin and subcutaneous tissue disorders			
Alopecia	1 (2.13%)	1 (6.67%)	2 (3.23%)
Dry skin	0 (0.00%)	1 (6.67%)	1 (1.61%)
Erythema	2 (4.26%)	1 (6.67%)	3 (4.84%)
Palmar-plantar erythrodysaesthesia syndrome	5 (10.64%)	3 (20.00%)	8 (12.90%)

Pruritus	3 (6.38%)	0 (0.00%)	3 (4.84%)
Rash	3 (6.38%)	1 (6.67%)	4 (6.45%)
Rash macular	0 (0.00%)	1 (6.67%)	1 (1.61%)
Rash maculo-papular	0 (0.00%)	1 (6.67%)	1 (1.61%)
Vascular disorders			
Hypertension	13 (27.66%)	3 (20.00%)	16 (25.81%)
Hypotension	0 (0.00%)	1 (6.67%)	1 (1.61%)

Other Relevant Findings

None

Conclusion:

The objective of this study was to evaluate the efficacy, safety and quality of life in subjects taking pazopanib after receiving prior ICIs, irrespective of the combination therapy in 1st and 2nd line setting. The study met its objective and showed a clinically meaningful PFS when pazopanib was administered as 2nd line in favorable risk group subjects. This suggests that treatment sequencing is crucial in management of advanced or metastatic RCC and patients may benefit from pazopanib treatment post progression after checkpoint inhibitor therapy.

No clinically meaningful decline in Quality-of-Life measures was observed, similar to results previously reported for pazopanib therapy.

The safety profile observed is similar to the previous experience with pazopanib and the adverse events are manageable

Date of Clinical Trial Report

Primary CSR: 17-Aug-2020; Final CSR: 21-Apr-2022