Clinical trial results:
A Phase II Study Investigating Upfront Pazopanib in Metastatic Clear Cell Renal Cancer [PANTHER]

Summary

EudraCT number	2009-016675-29
Trial protocol	GB
Global end of trial date	29 February 2016

Results information

Result version number	v1 (current)
This version publication date	07 April 2017
First version publication date	07 April 2017
Summary attachment (see zip file)	Journal Article (coi160025published 2.6.2016.pdf)

Trial information

Trial identification

Sponsor protocol code	RC200902

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01512186
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Queen Mary University London
Sponsor organisation address	5 Walden Street, London, United Kingdom, E1 2EF
Public contact	Thomas Powles, Centre for Experimental Cancer Medicine, bci-panther@qmul.ac.uk
Scientific contact	Thomas Powles, Centre for Experimental Cancer Medicine, bci-panther@qmul.ac.uk

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 December 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 February 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the clinical benefit of giving 14 weeks pazopanib to patients with metastatic kidney cancer prior to surgery to remove the cancerous kidney (nephrectomy).

Protection of trial subjects:

Patients were closely monitored as part of the clinical trial. Pazopanib was chosen as having a good effect in renal cancer, but with a lower toxicity profile than the similar, licensed, drug, sunitinib. Therefore the effect of the drug was well known, and the trial was looking at the effect on the surgery. The additional scans given as part of the trial were reassuring for the patients also.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 July 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 104
Worldwide total number of subjects	104
EEA total number of subjects	104

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)	48
From 65 to 84 years	45
85 years and over	11

Subject disposition

Recruitment

Recruitment details:

Between 6th July 2010 and 9 Dec 2015, 104 previously untreated patients with metastatic clear cell renal cancer were recruited to the PANTHER trial. This was a multicentre single-arm trial enrolling from 12 centres in the United Kingdom with nephrectomy services.

Pre-assignment

Screening details:

111 patients were screened for the trial, with 7 patients being ineligible.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Pazopanib

Arm description:

intervention arm (single)

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

Dosage and administration details:

800mg PO OD (2 x 400mg tablets)

Number of subjects in period 1	Pazopanib
Started	104
Completed	104

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial (overall period)
Reporting group description: Overall trial	

Reporting group values	Overall trial (overall period)	Total	
Number of subjects	104	104	
Age categorical Units: Subjects			
Adults (18-64 years)	48	48	
From 65-84 years	45	45	
85 years and over	0	0	
missing	11	11	
Age continuous Units: years			
median	63.8		
inter-quartile range (Q1-Q3)	56.3 to 70.8	-	
Gender categorical Units: Subjects			
Female	24	24	
Male	80	80	
not recorded	0	0	
MSKCC prognostic risk			
Memorial Sloan Kettering Cancer Center score			
Units: Subjects			
Good	0	0	
Intermediate	83	83	
Poor	18	18	
not recorded	3	3	
Performance status Units: Subjects			
Grade 0	29	29	
Grade 1	63	63	
Grade 2	9	9	
not recorded	3	3	
Type of surgery Units: Subjects			
Open	43	43	
Laparoscopic	18	18	
Complete	1	1	
Partial	1	1	
none	41	41	
T-stage at nephrectomy Units: Subjects			
T1	6	6	
T2	7	7	

T3	41	41	
T4	6	6	
no nephrectomy	41	41	
Not recorded	3	3	
Lung metastasis Units: Subjects			
yes	90	90	
no	14	14	
Bone metastasis Units: Subjects			
yes	29	29	
no	75	75	
Lymph node metastasis Units: Subjects			
yes	48	48	
no	56	56	
Liver metastasis Units: Subjects			
yes	15	15	
no	89	89	
Radiologic T stage at diagnosis Units: Subjects			
T1	10	10	
T2	29	29	
T3	52	52	
T4	11	11	
Not recorded	2	2	
Primary tumour size Units: cm			
median	10		
inter-quartile range (Q1-Q3)	8.3 to 11.6	-	

Subject analysis sets

Subject analysis set title	Pazopanib
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects

Subject analysis set title	clinical benefit
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Patients assessable for clinical benefit prior to planned nephrectomy.
Four patients were not assessable.

Reporting group values	Pazopanib	clinical benefit	
Number of subjects	104	100	
Age categorical Units: Subjects			
Adults (18-64 years)	48		
From 65-84 years	45		
85 years and over	0		

missing	11		

Age continuous			
Units: years			
median	63.8		
inter-quartile range (Q1-Q3)	56.3 to 70.8		
Gender categorical			
Units: Subjects			
Female	24		
Male	80		
not recorded	0		
MSKCC prognostic risk			
Memorial Sloan Kettering Cancer Center score			
Units: Subjects			
Good	0		
Intermediate	83		
Poor	18		
not recorded	3		
Performance status			
Units: Subjects			
Grade 0	29		
Grade 1	63		
Grade 2	9		
not recorded	3		
Type of surgery			
Units: Subjects			
Open	43		
Laparoscopic	18		
Complete	1		
Partial	1		
none	41		
T-stage at nephrectomy			
Units: Subjects			
T1	6		
T2	7		
T3	41		
T4	6		
no nephrectomy	41		
Not recorded	3		
Lung metastasis			
Units: Subjects			
yes	90		
no	14		
Bone metastasis			
Units: Subjects			
yes	29		
no	75		
Lymph node metastasis			
Units: Subjects			
yes	48		

no	56		
Liver metastasis Units: Subjects			
yes	15		
no	89		
Radiologic T stage at diagnosis Units: Subjects			
T1	10		
T2	29		
T3	52		
T4	11		
Not recorded	2		
Primary tumour size Units: cm			
median	10	10	
inter-quartile range (Q1-Q3)	8.3 to 11.6	8.3 to 11.6	

End points

End points reporting groups

Reporting group title	Pazopanib
Reporting group description: intervention arm (single)	
Subject analysis set title	Pazopanib
Subject analysis set type	Full analysis
Subject analysis set description: All subjects	
Subject analysis set title	clinical benefit
Subject analysis set type	Sub-group analysis
Subject analysis set description: Patients assessable for clinical benefit prior to planned nephrectomy. Four patients were not assessable.	

Primary: Clinical benefit

End point title	Clinical benefit
End point description: Percentage of patients who obtained clinical benefit at 14 weeks.	
End point type	Primary
End point timeframe: overall trial	

End point values	Pazopanib	clinical benefit		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	100	100		
Units: rate				
number (confidence interval 95%)	0.84 (0.75 to 0.91)	0.84 (0.75 to 0.91)		

Statistical analyses

Statistical analysis title	Clinical benefit
Statistical analysis description: number of patients that achieved clinical benefit	
Comparison groups	Pazopanib v clinical benefit
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	other[1]
Parameter estimate	rate
Point estimate	0.84

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	0.91

Notes:

[1] - this analysis does compare two groups, only estimates the overall clinical benefit in the 'clinical benefit' group

Secondary: Progression-free survival

End point title	Progression-free survival

End point description:

End point type	Secondary

End point timeframe:

Date of randomisation until disease progression or death from any cause.

End point values	Pazopanib	Pazopanib		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	104	104		
Units: months				
median (confidence interval 95%)	7.1 (6 to 9.2)	7.1 (6 to 9.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:

End point type	Secondary

End point timeframe:

Date of randomisation until death from any cause

End point values	Pazopanib	Pazopanib		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	104	104		
Units: months				
median (confidence interval 95%)	22.7 (14.3 to 99999999)	22.7 (14.3 to 99999999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Surgical complication

End point title	Surgical complication

End point description:

End point type	Secondary

End point timeframe:

Surgery complications observed from nephrectomy

End point values	Pazopanib	Pazopanib		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	63	63		
Units: Number of patients				
number (not applicable)				
Bleeding	5	5		
Delayed wound healing	4	4		
Splenectomy	2	2		
Elevated creatinine level	1	1		

Attachments (see zip file)	Nephrectomy data Table 1.docx

Statistical analyses

No statistical analyses for this end point

Secondary: Response to pazopanib treatment

End point title	Response to pazopanib treatment

End point description:

Median size of primary tumour before and after pazopanib treatment

End point type	Secondary

End point timeframe:

Length of pazopanib treatment

End point values	Pazopanib	Pazopanib		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	104	104		
Units: cm				
number (not applicable)				
Before Pazopanib	10	10		
After pazopanib	8.3	8.3		

Attachments (see zip file)	Percentage Change of Primary Tumour /Percentage change of

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Overall trial (overall period)

Assessment type	Non-systematic

Dictionary used

Dictionary name	CTC
Dictionary version	3.0

Reporting groups

Reporting group title	Pazopanib

Reporting group description: -

Serious adverse events	Pazopanib		
Total subjects affected by serious adverse events			
subjects affected / exposed	67 / 104 (64.42%)		
number of deaths (all causes)	52		
number of deaths resulting from adverse events			
Vascular disorders			
Vascular disorders			
subjects affected / exposed	4 / 104 (3.85%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
General disorders and administration site conditions			
subjects affected / exposed	8 / 104 (7.69%)		
occurrences causally related to treatment / all	1 / 10		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Reproductive system and breast disorders			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders			

subjects affected / exposed	11 / 104 (10.58%)		
occurrences causally related to treatment / all	1 / 13		
deaths causally related to treatment / all	0 / 2		
Psychiatric disorders			
Psychiatric disorders			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Investigations			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications			
subjects affected / exposed	12 / 104 (11.54%)		
occurrences causally related to treatment / all	3 / 13		
deaths causally related to treatment / all	0 / 2		
Cardiac disorders			
Cardiac disorders			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Nervous system disorders			
subjects affected / exposed	4 / 104 (3.85%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Blood and lymphatic system disorders			
subjects affected / exposed	5 / 104 (4.81%)		
occurrences causally related to treatment / all	3 / 6		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Gastrointestinal disorders			
subjects affected / exposed	15 / 104 (14.42%)		
occurrences causally related to treatment / all	8 / 19		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal and Urinary disorders			
subjects affected / exposed	9 / 104 (8.65%)		
occurrences causally related to treatment / all	1 / 10		
deaths causally related to treatment / all	0 / 1		
Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders			
subjects affected / exposed	4 / 104 (3.85%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infections and infestations			
subjects affected / exposed	5 / 104 (4.81%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	0 / 1		
Metabolism and nutrition disorders			
Metabolism and nutrition disorders			
subjects affected / exposed	6 / 104 (5.77%)		
occurrences causally related to treatment / all	2 / 6		
deaths causally related to treatment / all	0 / 1		

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

Non-serious adverse events	Pazopanib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	97 / 104 (93.27%)		
Investigations			
weight loss			
subjects affected / exposed	10 / 104 (9.62%)		
occurrences (all)	14		
Vascular disorders			
hypertension			
subjects affected / exposed	52 / 104 (50.00%)		
occurrences (all)	141		
General disorders and administration site conditions			
fatigue			
subjects affected / exposed	88 / 104 (84.62%)		
occurrences (all)	345		
pain			
subjects affected / exposed	33 / 104 (31.73%)		
occurrences (all)	87		
Gastrointestinal disorders			
constipation			
subjects affected / exposed	16 / 104 (15.38%)		
occurrences (all)	29		
diarrhoea			
subjects affected / exposed	55 / 104 (52.88%)		
occurrences (all)	222		
mucositis			
subjects affected / exposed	15 / 104 (14.42%)		
occurrences (all)	27		
nausea			
subjects affected / exposed	47 / 104 (45.19%)		
occurrences (all)	116		
taste change			
subjects affected / exposed	20 / 104 (19.23%)		
occurrences (all)	41		
vomiting			
subjects affected / exposed	20 / 104 (19.23%)		
occurrences (all)	39		

Skin and subcutaneous tissue disorders hand and foot syndrome subjects affected / exposed occurrences (all)	 33 / 104 (31.73%) 108		
Musculoskeletal and connective tissue disorders cramps subjects affected / exposed occurrences (all)	 10 / 104 (9.62%) 18		
Metabolism and nutrition disorders low appetite subjects affected / exposed occurrences (all)	 14 / 104 (13.46%) 22		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 May 2010	Addition of a thyroid function check 12-weeks prior to trial entry Expansion of exclusion criteria relating to cardiac function - 'Prolonged QT Interval >480msecs or a history of prolonged QT interval >480msecs' Post-surgery visit timepoints changed from 2,6,12 weeks to 4,8,12 weeks.
22 September 2010	Change of Principal Investigators only
06 September 2011	Additional of an exclusion criteria to prohibit patients to take part in the GE-135-009 study entering the PANTHER trial
04 April 2012	Removal of exclusion criteria prohibiting entry to the GE-135-009 study (this study never commenced). 6 weekly MRI changed to 4-weekly. Typographical error in PIS relating to IMP dosing.
22 May 2012	Addition of a central facility only
19 August 2014	Change of Principal Investigators only
12 February 2015	Removal of central review from protocol Clarification of end of study definition and analysis timepoints
04 February 2016	Change of Principal Investigator only

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/27254750