Clinical trial results:
Improving the tolerability of the oral targeted anti-cancer drug pazopanib by food intake (DIET)

Summary

EudraCT number	2013-004108-20
Trial protocol	NL
Global end of trial date	09 August 2018

Results information

Result version number	v1 (current)
This version publication date	26 January 2020
First version publication date	26 January 2020

Trial information

Trial identification

Sponsor protocol code	UMCN-AKF13.05

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02138526
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Radboudumc
Sponsor organisation address	Geert Grooteplein Zuid 10, Nijmegen, Netherlands,
Public contact	Angela Colbers, Radboud University Nijmegen Medical Centre, +31 243616405, angela.colbers@radboudumc.nl
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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	15 November 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 August 2018
Global end of trial reached?	Yes
Global end of trial date	09 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Part A: To determine the equivalent dose of pazopanib when taken with a continental breakfast compared to 800 mg in fasted state.
Part B:To evaluate whether food can reduce the side effects diarrhea and nausea.

Protection of trial subjects:

Part A
Participating patients will be asked for a hospital admission for two days to collect the blood samples. All blood samples will be drawn from a once placed intravenous cannula. A total of 10 blood samples will be taken per admission day. the burden for the participants of this part of the study is considered to be mild. In general the risk for participation in this study is regarded moderate.
The risk of suboptimal dosing is minimized by the run in of three patients at 600 mg OD with food.
Benefits associated with participating in this study are that patients and their treating physician get insight into pazopanib exposure when taken with a continental breakfast.
Part B
The participating patients are asked to keep a record on their defecation pattern and nausea experiences during both treatment regiments, at the end of the study period their preference is asked. Therefore the burden for the participants of this part of the study is considered to be low.
In general the risk for participation in this study is regarded negligible.
Patient receive a bioequivalent dose pazopanib also normal Ctrhough levels will be monitored.
Benefits associated with participating in this study are that patients might experience less side effects and the intake of pazopanib will be more easily incorporated in their normal life style.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 January 2014
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	Netherlands: 97
Worldwide total number of subjects	97
EEA total number of subjects	97

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	68
From 65 to 84 years	28
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

This study was conducted in two parts. First, a PK study was performed to establish the bioequivalent dose of pazopanib when ingested with a CB (part 1). This part was designed as an open-label, crossover, multicenter, phase I study conducted in two centers in the Netherlands (Radboudumc (Nijmegen) and Leiden University Medical Center (Leiden).

Pre-assignment

Screening details:

Adult patients (≥ 18 years) receiving 800 mg pazopanib o.d. with an ECOG performance status of 0−2. The use of proton pump inhibitors was allowed when the proton pump inhibitor was used at the same time throughout the study. Use of substances known to alter Cytochrome P 3A4 metabolism were prohibited. Patients with GI abnormalities were excluded.

Period 1

Period 1 title	screening
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

nap

Arms

Arm title	baseline

Arm description:

baseline

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

Dosage and administration details:

800mg once daily oral without food

Number of subjects in period 1	baseline
Started	97
Completed	78
Not completed	19
Lost to follow-up	1
Lack of efficacy	18

Period 2	
Period 2 title	PKcurves
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	No
Arm title	pazopanib 800mg fasting

Arm description:
pazopanib 800mg fasting

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

Dosage and administration details:
800mg once daily oral without food

Arm title	pazopanib 600mg + food

Arm description:
pazopanib 600mg + food

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

Dosage and administration details:
600mg once daily oral with food

Number of subjects in period 2	pazopanib 800mg fasting	pazopanib 600mg + food
Started	78	78
Completed	78	78

Baseline characteristics

Reporting groups	
Reporting group title	screening

Reporting group description: -

Reporting group values	screening	Total	
Number of subjects	97	97	
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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
median	60		
full range (min-max)	28 to 85	-	
Gender categorical Units: Subjects			
Female	30	30	
Male	67	67	

End points

End points reporting groups	
Reporting group title	baseline
Reporting group description: baseline	
Reporting group title	pazopanib 800mg fasting
Reporting group description: pazopanib 800mg fasting	
Reporting group title	pazopanib 600mg + food
Reporting group description: pazopanib 600mg + food	

Primary: AUC	
End point title	AUC
End point description:	
End point type	Primary
End point timeframe: 24h	

End point values	pazopanib 800mg fasting	pazopanib 600mg + food		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	78		
Units: mg*h/L				
geometric mean (geometric coefficient of variation)	821 (± 36)	895 (± 38)		

Statistical analyses

Statistical analysis title	GMR
Comparison groups	pazopanib 800mg fasting v pazopanib 600mg + food
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	equivalence[1]
P-value	< 0.1 [2]
Method	Mixed models analysis
Parameter estimate	Median difference (final values)
Point estimate	1.09

Confidence interval	
level	90 %
sides	2-sided
lower limit	1.02
upper limit	1.17

Notes:

[1] - intrasubject comparison, not 156 different subjects in analysis

[2] - nap

Adverse events

Adverse events information	
Timeframe for reporting adverse events: entire study	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	none
Dictionary version	1
Reporting groups	
Reporting group title	all patients

Reporting group description: -

Serious adverse events	all patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 79 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	all patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 79 (7.59%)		
Cardiac disorders			
hypertension			
subjects affected / exposed	3 / 79 (3.80%)		
occurrences (all)	3		
General disorders and administration site conditions			
fatigue			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences (all)	1		
hair discoloration			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences (all)	1		
Pain			

subjects affected / exposed occurrences (all)	1 / 79 (1.27%) 1		
Respiratory, thoracic and mediastinal disorders pneumonia subjects affected / exposed occurrences (all)	 1 / 79 (1.27%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 June 2018	1. Change in in- and exclusion criteria When according to the treating physician a patient is eligible for pazopanib treatment, the patient is eligible for study participation. 2. Added secondary objective Progression free survival was added as an secondary objective.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported