

**Clinical trial results:
Increasing pazopanib exposure by splitting intake moments
Summary**

EudraCT number	2016-005252-21
Trial protocol	NL
Global end of trial date	12 March 2019

Results information

Result version number	v1 (current)
This version publication date	22 February 2021
First version publication date	22 February 2021
Summary attachment (see zip file)	Groenland et al (Clin Pharmacokinet, 2020) - pazopanib split intake (Groenland et al (Clin Pharmacokinet, 2020) - pazopanib split intake.pdf)

Trial information**Trial identification**

Sponsor protocol code	N17PSI
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	CCMO dossier number: NL60393.031.17, NL trialregister: NL6137

Notes:

Sponsors

Sponsor organisation name	Netherlands Cancer Institute
Sponsor organisation address	Plesmanlaan 121, Amsterdam, Netherlands, 1066CX
Public contact	Steffie Groenland, Netherlands Cancer Institute, s.groenland@nki.nl
Scientific contact	Steffie Groenland, Netherlands Cancer Institute, s.groenland@nki.nl

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	20 December 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 January 2019
Global end of trial reached?	Yes
Global end of trial date	12 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To show whether switching patients from a once daily (QD) to a twice daily (BID) dosing schedule will lead to a significant increase in pharmacokinetic exposure, measured as C_{min} and AUC_{0-24h}.

Protection of trial subjects:

Theoretically, a possible risk of additional toxicity exists, as we expect an increase in exposure by splitting intake moments of pazopanib. However, this risk is minimized by:

- The short duration of the intervention (only seven days);
- The exclusion of patients with a high C_{min} at screenin

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 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	Netherlands: 11
Worldwide total number of subjects	11
EEA total number of subjects	11

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)	7
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients with histological or cytological proof of cancer with an indication for treatment with pazopanib (i.e., advanced RCC or STS) were eligible for inclusion. Since evidence suggests pazopanib exposure may drop during the first weeks of treatment, all patients needed to be on pazopanib 800 mg QD treatment \geq 3 weeks prior to start of the study.

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	Arm1
Arm description: -	
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:

Cross-over pazopanib 800 mg QD or pazopanib 400 mg twice daily

Number of subjects in period 1	Arm1
Started	11
Completed	9
Not completed	2
In one patient, pazopanib treatment was interrupted	2

Baseline characteristics

Reporting groups

Reporting group title

Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	11	11	
Age categorical			
Age			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	7	7	
From 65-84 years	4	4	
85 years and over	0	0	
adults	0	0	
Gender categorical			
gender			
Units: Subjects			
Female	8	8	
Male	3	3	

End points

End points reporting groups

Reporting group title	Arm1
Reporting group description: -	

Primary: The primary endpoint of this study was to evaluate whether switching patients from an 800 mg QD to a 400 mg BID dosing schedule would lead to an increase in pharmacokinetic exposure, measured as Cmin and area under the concentration– time curve from zero

End point title	The primary endpoint of this study was to evaluate whether switching patients from an 800 mg QD to a 400 mg BID dosing schedule would lead to an increase in pharmacokinetic exposure, measured as Cmin and area under the concentration– time curve from zero ^[1]
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End point description:

End point type	Primary
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End point timeframe:

Time points at day 1 (800 mg QD) were pre-dose and 1, 2, 3, 4, 5, 6, 8, 10, 12, and 24 h post-dose.
Time points at day 8 (400 mg BID) were predose and 1, 2, 3, 4, 5, 6, 8, 10, 12, 13, 14, 15, 16, and 24 h post-dose.

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: See table 2 of publication attached

End point values	Arm1			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: mg/L and h/L				
number (not applicable)	9			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Adverse events should be collected beginning from day 1 of the study and ending with the end of the study.

Assessment type	Systematic
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Dictionary used

Dictionary name	CTC
Dictionary version	4.03

Frequency threshold for reporting non-serious adverse events: 1 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: See table 3 of publication attached.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 June 2017	Erasmus Medical Center added as trial center. Change in data collection (eCRF) Clarification in SAE reporting procedures.
03 July 2018	-New independent physician -New privacy legislation

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported