EU Clinical Trials Register

Clinical trial results:
A randomized phase II study to explore the efficacy and feasibility of upfront bi-monthly rotations between Everolimus and Pazopanib with sequential treatment of first line Pazopanib and second line Everolimus until progression in patients with advanced or metastatic clear cell renal cancer.

Summary

EudraCT number	2011-000127-32
Trial protocol	NL
Global end of trial date	05 April 2016

Results information

Result version number	v1 (current)
This version publication date	15 June 2022
First version publication date	15 June 2022
Summary attachment (see zip file)	Statistical report (M2. Statistical Report dd 22-06-2018.pdf)

Trial information

Trial identification

Sponsor protocol code	ROPETAR

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01408004
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	WIN-O
Sponsor organisation address	Postbus 821, Zeist, Netherlands, 3700 AV
Public contact	Medical oncology/G.A. Cirkel, UMC Utrecht, +31 887556265, g.a.cirkel-2@umcutrecht.nl
Scientific contact	Medical oncology/G.A. Cirkel, UMC Utrecht, +31 887556265, g.a.cirkel-2@umcutrecht.nl
Sponsor organisation name	WIN-O
Sponsor organisation address	Postbus 821, Zeist , Netherlands, 3700 AV
Public contact	Jeanine Eikmans, WIN-O, +31 639488702 , nfo@win-o.nl
Scientific contact	Jeanine Eikmans, I WIN-O, +31 639488702 , info@win-o.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	11 March 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 March 2016
Global end of trial reached?	Yes
Global end of trial date	05 April 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to assess the progression-free survival of patients who receive bi-monthly rotations of Pazopanib and Everolimus versus patients who receive Pazopanib as a first line treatment.

Protection of trial subjects:

NA

Background therapy:

NA

Evidence for comparator:

COMPARZ trial

Actual start date of recruitment	15 July 2011
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	Netherlands: 101
Worldwide total number of subjects	101
EEA total number of subjects	101

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)	60
From 65 to 84 years	41

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Within time limits, between September 2012 and April 2014

Pre-assignment

Screening details:

NA

Period 1

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

Blinding implementation details:

NA

Arms

Are arms mutually exclusive?	Yes
Arm title	Experimental

Arm description:

Experimental: rotating treatment

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

Dosage and administration details:

800mg 1dd 8 weeks (rotating)

Investigational medicinal product name	everolimus
Investigational medicinal product code	
Other name	afinitor
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

10 mg QD, 8 weeks, rotating

Arm title	Comparator

Arm description:

pazopaninbg until PD, then everolimus

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

Dosage and administration details:

800mg QD until PD

Investigational medicinal product name	Everolimus
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

10 mg QD, until PD

Number of subjects in period 1	Experimental	Comparator
Started	52	49
Completed	52	49

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	101	101	
Age categorical			
Age Median Experimental: 65 Comparator: 67 Overall: 66 0% 25% 75% 100% quantile Experimental: 44 59 71 87 Comparator: 38 58 72 82 Overall: 38 58 72 87 Mean 65 65 65 Standard Deviation 10 10 10			
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)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age > 18 years	101	101	
Gender categorical Units: Subjects			
Female	32	32	
Male	69	69	
Reference			
Please refer to JAMA Oncol. 2017;3(4):501-508 for a complete overview of baseline characteristics			
Units: Subjects			
Link to paper	101	101	

End points

End points reporting groups

Reporting group title	Experimental
Reporting group description:	
Experimental: rotating treatment	
Reporting group title	Comparator
Reporting group description:	
pazopaninbg until PD, then everolimus	

Primary: Progression free survival

End point title	Progression free survival
End point description:	
survival until first progression or death.	
End point type	Primary
End point timeframe:	
Randomisation to survival until first progression or death.	

End point values	Experimental	Comparator		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	49		
Units: month				
median (confidence interval 95%)	7.4 (5.6 to 18.4)	9.4 (6.6 to 11.9)		

Attachments (see zip file)	Charts in paper/jamaoncology_cirkel_2016_oi_160080 (1) (1)

Statistical analyses

Statistical analysis title	Statistical Methods

Statistical analysis description:

A total sample size of 100 patients was planned. From literature it was estimated that the 1-year PFS1 in the control arm would be 50%. An increase from 50% to 80% 1-year PFS of the rotating schedule over standard of care with first-line VEGFR-TKI was considered to be clinically relevant. Primary analysis was planned when over 60 events (first progression or death) were recorded, enabling detection of an increase in 1-year PFS to 80% (power 90%, α=.05, 2-tailed test).

Comparison groups	Experimental v Comparator
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	Regression, Cox
Parameter estimate	Median difference (final values)
Point estimate	50

Confidence interval	
level	95 %
sides	2-sided
lower limit	50
upper limit	80
Variability estimate	Standard deviation
Dispersion value	0

Adverse events

Adverse events information

Timeframe for reporting adverse events:	
Time between first drug dose and 30 days after EOT	
Adverse event reporting additional description:	
NA	
Assessment type	Systematic

Dictionary used

Dictionary name	CTC
Dictionary version	4.03

Reporting groups

Reporting group title	Experimental
Reporting group description:	
Experimental: rotating treatment	
Reporting group title	Comparator
Reporting group description:	
pazopanib until PD, then everolimus	

Serious adverse events	Experimental	Comparator	
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 52 (42.31%)	24 / 49 (48.98%)	
number of deaths (all causes)	5	7	
number of deaths resulting from adverse events	2	2	
Investigations			
Adverse event	Additional description: It;s impossible to enter all SAEs manually. Please refer to fullpaper: JAMA Oncol. 2017;3(4):501-508 and separate uploaded PDF with all AEs/SAEs details		
subjects affected / exposed	22 / 52 (42.31%)	24 / 49 (48.98%)	
occurrences causally related to treatment / all	22 / 22	24 / 24	
deaths causally related to treatment / all	0 / 2	1 / 2	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Experimental	Comparator	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 52 (100.00%)	49 / 49 (100.00%)	
Investigations			
Adverse event			

subjects affected / exposed	52 / 52 (100.00%)	49 / 49 (100.00%)	
occurrences (all)	52	49	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol?   No

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.

Not all required data are available and/or impossible to enter in this overview. PLEASE REFER TO FULL PAPER IN JAMA ONCOLOGY OR ATTACHED STATISTICAL REPORT FOR VALIDATED DATA

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/27918762