Clinical trial results:
Pharmacokinetics of posaconazole (Noxafil(R)) as prophylaxis for invasive fungal disease

Summary

EudraCT number	2016-001182-87
Trial protocol	NL BE
Global end of trial date	09 February 2019

Results information

Result version number	v1 (current)
This version publication date	19 March 2020
First version publication date	19 March 2020

Trial information

Trial identification

Sponsor protocol code	UMCN-AKF16.01

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Radboudumc
Sponsor organisation address	Geert Grooteplein Zuid 10, Nijmegen, Netherlands, 6525 GA
Public contact	Roger Brüggemann, Radboud University Medical Centre, +31 243616405, roger.bruggemann@radboudumc.nl
Scientific contact	Roger Brüggemann, Radboud University Medical Centre, +31 243616405, r.bruggemann@akf.umcn.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	03 February 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 February 2019
Global end of trial reached?	Yes
Global end of trial date	09 February 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To determine the pharmacokinetics of posaconazole (new solid oral and IV) given as prophylaxis to patients who are at risk for developing fungal infections after receiving immunosuppressive therapy for acute GVHD, (non)myeloablative or reduced intensity conditioning regimens for SCT, or remission induction chemotherapy for AML/MDS.
- To determine the oral bioavailability and specific the impact of mucositis on changes in drug absorption or presystemic clearance.

Protection of trial subjects:

This study uses posaconazole, which is an antifungal agent licensed for prophylaxis as well treatment of invasive fungal infections. The dosages and clinical indications used in this trial are similar to the licensed dosages or lower; therefore no potential harmful risks are expected in this cohort. Furthermore, the study medication, posaconazole, given as antifungal prophylaxis is given on top of standard intensive diagnostic work-up to detect a fungal infection as soon as possible.

The burden of the patient is identical to studies previously performed in the same cohort (voriconazole, anidulafungin and micafungin, all approved by the ethics committee). We strongly believe the burden for the patient as well as the risk for severe adverse events is reduced to an absolute minimum.

The risk-classification is assessed as negligible to the patient population receiving study drug at the current regimens. The drug is licensed for the use investigated in this protocol. Safety data on the use of higher dose are published and very-well defined. There is no attributable risk for the application of the study protocol to the haematology patients at risk for fungal infections.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 2016
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: 15
Country: Number of subjects enrolled	Belgium: 12
Worldwide total number of subjects	27
EEA total number of subjects	27

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)	17
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment took place from August 2016 to 08-06-2019 in Nijmegen, Netherlands and Leuven in Belgium.

Pre-assignment

Screening details:

Patient receives immunosuppressive therapy for acute GVHD grade II-IV, reduced intensity conditioning regimens for allogeneic stem cell transplant, or first remission induction chemotherapy for AML/MDS. In case of acute GVHD grade II-IV, patient has received less than 1 week of immunosuppressive therapy. ASAT <200U/L, ALAT <225U/L, AP <460U/L

Period 1

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

Arms

Arm title	all patients

Arm description: -

Arm type	none
Investigational medicinal product name	posaconazole not yet started
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

no dose administered at screening

Number of subjects in period 1	all patients
Started	27
Completed	27

Period 2

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

Arms

Are arms mutually exclusive?	Yes

Arm title	posa ref
Arm description:	
posaconazole iv treatment	
Arm type	Active comparator
Investigational medicinal product name	posaconazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

posaconazole IV 300mg BID on the first day (posaconazole will be infused over a period of 90 minutes), days 2-7 patients will receive posaconazole IV 300mg QD.

Arm title	posa oral
Arm description:	
posaconazol oral	
Arm type	Experimental
Investigational medicinal product name	posaconazole oral
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

posaconazole PO 300mg BID on the first day, days 2-7: patients will receive posaconazole PO 300mg QD.

Number of subjects in period 2	posa ref	posa oral
Started	13	14
Completed	13	14

Baseline characteristics

Reporting groups	
Reporting group title	screening
Reporting group description:	
screened patients	

Reporting group values	screening	Total	
Number of subjects	27	27	
Age categorical			
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)	17	17	
From 65-84 years	10	10	
85 years and over	0	0	
Gender categorical			
gender			
Units: Subjects			
Female	15	15	
Male	12	12	

Subject analysis sets	
Subject analysis set title	all subjects
Subject analysis set type	Full analysis
Subject analysis set description:	
subjects for demographics	

Reporting group values	all subjects		
Number of subjects	27		
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)	17		
From 65-84 years	10		
85 years and over			

Gender categorical			
gender			
Units: Subjects			
Female	15		
Male	12		

End points

End points reporting groups

Reporting group title	all patients
Reporting group description: -	
Reporting group title	posa ref
Reporting group description: posaconazole iv treatment	
Reporting group title	posa oral
Reporting group description: posaconazol oral	
Subject analysis set title	all subjects
Subject analysis set type	Full analysis
Subject analysis set description: subjects for demographics	

Primary: posa AUC0-24h

End point title	posa AUC0-24h[1]
End point description:	
End point type	Primary
End point timeframe: 24hour after observed dosing	

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: no formal analysis was done

End point values	posa ref	posa oral		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13[2]	14		
Units: mg*h/L				
median (inter-quartile range (Q1-Q3))	43 (36 to 55)	33 (19 to 41)		

Notes:

[2] - should be 17, as intrasubject

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

entire study

Adverse event reporting additional description:

SAE

Assessment type	Systematic

Dictionary used

Dictionary name	none
Dictionary version	1

Reporting groups

Reporting group title	all subjects

Reporting group description: -

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: no non-serious AEs were reported

Serious adverse events	all subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 27 (14.81%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Hypokalaemic syndrome			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
QTc prolongation			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
hypotension			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	all subjects		
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 27 (0.00%)		

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

None reported