Clinical trial results:
Pharmacokinetics of micafungin (Mycamin ®) as antifungal prophylaxis given twice weekly intravenously compared to micafungin given daily to patients at risk for developing an invasive fungal disease.

Summary

EudraCT number	2013-002848-93
Trial protocol	NL BE
Global end of trial date	30 May 2016

Results information

Result version number	v1 (current)
This version publication date	04 October 2020
First version publication date	04 October 2020
Summary attachment (see zip file)	MATADOR paper (MATADOR_JAC_paper_2018.pdf)

Trial information

Trial identification

Sponsor protocol code	UMCN-AKF13.02

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 10, Nijmegen, Netherlands,
Public contact	Roger Brüggemann, Radboud University Medical Centre, +31 243616405, roger.bruggemann@radboudumc.nl
Scientific contact	Roger Brüggemann, Radboud University Medical Centre, +31 243616405, roger.bruggemann@radboudumc.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	21 December 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 May 2016
Global end of trial reached?	Yes
Global end of trial date	30 May 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To determine the pharmacokinetics of micafungin 300 mg given twice weekly on Mondays and Thursdays in patients at risk for developing an invasive fungal disease (patients who are being treated for acute or chronic graft versus host disease; patients receiving reduced intensity conditioning for SCT; receiving first remission induction chemotherapy for AML/MDS) compared to the pharmacokinetics of micafungin 100 mg given daily to the same population.

Protection of trial subjects:

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	02 December 2013
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: 9
Country: Number of subjects enrolled	Belgium: 11
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	18

From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

recruitment in IC.

Pre-assignment

Screening details:

The included patientswere receiving immunosuppressive therapy for acute graft-versus-host disease (aGVHD) grade II–IV, undergoing reducedintensity
conditioning regimens for allogeneic HSCT, or receiving first remission-induction chemotherapy for AML/myelodysplastic syndrome (MDS), who were at least 18years of age, if female were not pregnant.

Pre-assignment period milestones

Number of subjects started	20
Number of subjects completed	20

Period 1

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

Blinding implementation details:

not applicable

Arms

Arm title	screening

Arm description:

screening

Arm type	no intervention
Investigational medicinal product name	micafungin screening
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

in the screening period no micafungin was given

Number of subjects in period 1	screening
Started	20
Completed	20

Period 2

Period 2 title	900 mg mica
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:
not applicable

Arms

Arm title	mica 900mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	micafungin 900mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:
300mg of micafungin twice weekly for 8 days (Group A, receiving 900mg in total

Number of subjects in period 2	mica 900mg
Started	20
Completed	20

Period 3

Period 3 title	mica 800mg
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:
not applicable

Arms

Arm title	mica 800mg
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	micafungin 800mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

100mg of micafungin once daily for 8 days

Number of subjects in period 3	mica 800mg
Started	20
Completed	19
Not completed	1
CVC removed	1

Baseline characteristics

Reporting groups	
Reporting group title	screening

Reporting group description: -

Reporting group values	screening	Total	
Number of subjects	20	20	
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	59.5		
full range (min-max)	36 to 68	-	
Gender categorical Units: Subjects			
Female	8	8	
Male	12	12	

End points

End points reporting groups

Reporting group title	screening
Reporting group description: screening	
Reporting group title	mica 900mg
Reporting group description: -	
Reporting group title	mica 800mg
Reporting group description: -	

Primary: area under the curve

End point title	area under the curve[1]
End point description:	
End point type	Primary
End point timeframe: 0-168 hours	

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 statistical test was done to compare, only descriptive

End point values	mica 900mg	mica 800mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	19		
Units: mg*h/L				
median (inter-quartile range (Q1-Q3))	690 (538 to 829)	596 (485 to 717)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

entire study

Assessment type	Systematic

Dictionary used

Dictionary name	none
Dictionary version	1

Reporting groups

Reporting group title	entire group

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: none reported

Serious adverse events	entire group		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 20 (30.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Blood and lymphatic system disorders			
CVC-ralted thrombosis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
neutropenic enterocolitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Respiratory, thoracic and mediastinal disorders			
respiratory insufficiency			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
pulmonary rhizomucor infection			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
renal insufficiency			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
painfull arthritis wrist			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Eppstein Barr virus reactivation			
subjects affected / exposed	1 / 20 (5.00%)		
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	entire group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 20 (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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/30137340