Clinical trial results:
Liposomal amphotericin B (Ambisome) pharmacokinetics given as a single intravenous dose to obese patients (ASPEN).

Summary

EudraCT number	2014-003306-33
Trial protocol	NL
Global end of trial date	03 November 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-AKF-14.04

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,
Public contact	Roger Brüggemann, Radboud university medical center, +31 243616405, roger.bruggemann@radboudumc.nl
Scientific contact	Roger Brüggemann, Radboud university medical center, +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	01 May 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 November 2018
Global end of trial reached?	Yes
Global end of trial date	03 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To determine the pharmacokinetics of liposomal amphotericin B administered as a single, intravenous dose (2 mg/kg or 3 mg/kg) to obese patients with a BMI ≥ 40 kg/m2.

Protection of trial subjects:

The risks for participating in this study are considered to be minimal. There are no direct benefits of this study for the study patients. The results of the study will provide insight into the pharmacokinetics of AmBisome in morbidly obese patients.
The first group of patients will receive a lower dose of 1 mg/kg. An interim analysis of the safety profile of the first group will be performed by the study team before proceeding to the 2 mg/kg dose group.
The dosages in our trial design (1 mg/kg and 2 mg/kg) are lower than the recommended dose by the manufacturer of 5 mg/kg (for treatment of invasive fungal infections caused by Aspergillus-species. Guidelines (ECIL, IDSA, SWAB) suggest 3 mg/kg for this indication) and 10 mg/kg used in Mucor species infections. Furthermore, the maximum tolerated dosage of AmBisome exceeds 15 mg/kg per day and was considered well tolerated.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 March 2018
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: 16
Worldwide total number of subjects	16
EEA total number of subjects	16

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)	16
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

morbidly obese but otherwise healthy adults with a body mass index (BMI >40 kg/m2) the day before they underwent bariatric surgery.

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

Are arms mutually exclusive?	Yes
Arm title	1 mg/kg group

Arm description: -

Arm type	Experimental
Investigational medicinal product name	AmBisome
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

no dose at screening

Arm title	2 mg/kg group

Arm description: -

Arm type	Experimental
Investigational medicinal product name	AmBisome
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

no dose at screening

Number of subjects in period 1	1 mg/kg group	2 mg/kg group
Started	8	8
Completed	8	8

Period 2	
Period 2 title	PK curve period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	Yes
Arm title	ambisome 1mg/kg

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	AmBisome
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:
1mg/kg ambisome IV single dose

Arm title	2 mg/kg ambisome

Arm description: -

Arm type	Experimental
Investigational medicinal product name	AmBisome
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:
2mg/kg ambisome IV single dose

Number of subjects in period 2	ambisome 1mg/kg	2 mg/kg ambisome
Started	8	8
Completed	8	8

Baseline characteristics

Reporting groups	
Reporting group title	1 mg/kg group
Reporting group description: -	
Reporting group title	2 mg/kg group
Reporting group description: -	

Reporting group values	1 mg/kg group	2 mg/kg group	Total
Number of subjects	8	8	16
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	34	39	
full range (min-max)	21 to 56	27 to 63	-
Gender categorical Units: Subjects			
Female	7	5	12
Male	1	3	4

End points

End points reporting groups

Reporting group title	1 mg/kg group
Reporting group description: -	
Reporting group title	2 mg/kg group
Reporting group description: -	
Reporting group title	ambisome 1mg/kg
Reporting group description: -	
Reporting group title	2 mg/kg ambisome
Reporting group description: -	

Primary: AUC

End point title	AUC[1]

End point description:

End point type	Primary

End point timeframe:

24h, no acutal AUCs were generated. PopPK model was generated. AUC values reported here are relative

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: not done, the results of this study do not fit into the template for reporting

End point values	ambisome 1mg/kg	2 mg/kg ambisome		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: mg*h/L				
geometric mean (geometric coefficient of variation)	1 (± 37)	2 (± 37)		

Statistical analyses

No statistical analyses for this end point

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 subjects

Reporting group description: -

Serious adverse events	all subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (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 subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 16 (87.50%)		
General disorders and administration site conditions			
red, warm skin			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
ache			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
hypertensia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
hot flushes			

subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2		
Musculoskeletal and connective tissue disorders muscle ache subjects affected / exposed occurrences (all)	 13 / 16 (81.25%) 14		

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/31588493