# 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<br>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<br>Units: years | | | |
| median | 34 | 39 | |
| full range (min-max) | 21 to 56 | 27 to 63 | - |
| Gender categorical<br>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<br>occurrences (all) | 2 / 16 (12.50%)<br>2 | | |
| Musculoskeletal and connective tissue disorders<br>muscle ache<br>subjects affected / exposed<br>occurrences (all) | <br><br>13 / 16 (81.25%)<br>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