Clinical trial results:
WIRKORTKONZENTRATIONEN VON AMPHOTERICIN B FORMULIERUNGEN IN ASZITES, LIQUOR, PLEURAERGUSS, GALLE UND LIQUOR BEI KRITISCH KRANKEN

(Target-site concentrations of Amphotericin B preparations in ascites, pleural effusion, bile and cerebrospinal fluid in critically ill patients)

Summary

EudraCT number	2007-001795-37
Trial protocol	AT
Global end of trial date	01 March 2016

Results information

Result version number	v1 (current)
This version publication date	01 September 2022
First version publication date	01 September 2022

Trial information

Trial identification

Sponsor protocol code	AMB TS

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medical University Innsbruck
Sponsor organisation address	Christoph-Probst-Platz 1, Innrain 52, Innsbruck, Austria, 6020
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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 March 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 March 2016
Global end of trial reached?	Yes
Global end of trial date	01 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

to determine concentrations of amphotericin B in plasma and at target site (ascites, pleural effusion, bile and cerebrospinal fluid).

to determine target-site penetration of amphotericin B preparatations administered in critically ill patients requiring a amphotericin B preparation.

Protection of trial subjects:

As the body fluid samples were drawn during routine interventions, there was no additional risk for the patients

Background therapy:

Subjects received treatment at the intensive care unit according to clinical requirements.

Evidence for comparator:

There was no evidence for a comparator in this trial.

Actual start date of recruitment	20 July 2007
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	Austria: 14
Worldwide total number of subjects	14
EEA total number of subjects	14

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	9
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Critically ill adult patients with a clinical indication for paracentesis (or peritoneal drainage), thoracentesis (or pleural drainage), lumbar puncture or bile deviation receiving treatment with lipid-formulated AmB for proven or suspected invasive fungal infection were enrolled.

Pre-assignment

Screening details:

Critically ill adult patients with a clinical indication for paracentesis (or peritoneal drainage), thoracentesis (or pleural drainage), lumbar puncture or bile deviation receiving treatment with lipid-formulated AmB for proven or suspected invasive fungal infection were enrolled.

Period 1

Period 1 title	Treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Ascites

Arm description:

Determination of Amphotericin B levels in ascitic specimens using High Performance Liquid Chromatography

Arm type	Experimental
Investigational medicinal product name	Amphocil
Investigational medicinal product code	ABCD
Other name	Amphotericin B colloidal dispersion
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

ABCD (Amphocil; Torrex-Chiesi Pharma, Vienna, Austria) was dissolved as recommended by the manufacturers and administered intravenously at doses of 3 to 5 mg/kg of body weight over 4 h once a day.

Investigational medicinal product name	AmBisome
Investigational medicinal product code	LAMB
Other name	Liposomal Amphotericin B
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

LAMB (AmBisome; Gilead, San Dimas, CA), was dissolved as recommended by the manufacturers and administered intravenously at doses of 3 to 5 mg/kg of body weight over 4 h once a day.

Investigational medicinal product name	Abelcet
Investigational medicinal product code	ABLC
Other name	Amphotericin B lipid complex
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

ABLC (Abelcet; Elan Pharma International Limited, Athlone, Ireland) was dissolved as recommended by the manufacturers and administered intravenously at doses of 3 to 5 mg/kg of body weight over 4 h once a day.

Arm title	Pleural effusion

Arm description:

Determination of Amphotericin B levels in pleural effusion specimens using High Performance Liquid Chromatography

Arm type	Experimental
Investigational medicinal product name	Amphocil
Investigational medicinal product code	ABCD
Other name	Amphotericin B colloidal dispersion
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

ABCD (Amphocil; Torrex-Chiesi Pharma, Vienna, Austria) was dissolved as recommended by the manufacturers and administered intravenously at doses of 3 to 5 mg/kg of body weight over 4 h once a day.

Investigational medicinal product name	AmBisome
Investigational medicinal product code	LAMB
Other name	Liposomal Amphotericin B
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

LAMB (AmBisome; Gilead, San Dimas, CA), was dissolved as recommended by the manufacturers and administered intravenously at doses of 3 to 5 mg/kg of body weight over 4 h once a day.

Investigational medicinal product name	Abelcet
Investigational medicinal product code	ABLC
Other name	Amphotericin B lipid complex
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

ABLC (Abelcet; Elan Pharma International Limited, Athlone, Ireland) was dissolved as recommended by the manufacturers and administered intravenously at doses of 3 to 5 mg/kg of body weight over 4 h once a day.

Arm title	Bile

Arm description:

Determination of Amphotericin B levels in bile specimens using High Performance Liquid Chromatography

Arm type	Experimental
Investigational medicinal product name	Amphocil
Investigational medicinal product code	ABCD
Other name	Amphotericin B colloidal dispersion
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

ABCD (Amphocil; Torrex-Chiesi Pharma, Vienna, Austria) was dissolved as recommended by the manufacturers and administered intravenously at doses of 3 to 5 mg/kg of body weight over 4 h once a day.

Investigational medicinal product name	AmBisome
Investigational medicinal product code	LAMB
Other name	Liposomal Amphotericin B
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

LAMB (AmBisome; Gilead, San Dimas, CA), was dissolved as recommended by the manufacturers and administered intravenously at doses of 3 to 5 mg/kg of body weight over 4 h once a day.

Investigational medicinal product name	Abelcet
Investigational medicinal product code	ABLC
Other name	Amphotericin B lipid complex
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

ABLC (Abelcet; Elan Pharma International Limited, Athlone, Ireland) was dissolved as recommended by the manufacturers and administered intravenously at doses of 3 to 5 mg/kg of body weight over 4 h once a day.

Number of subjects in period 1	Ascites	Pleural effusion	Bile
Started	3	7	4
Completed	3	7	4

Baseline characteristics

Reporting groups	
Reporting group title	Ascites
Reporting group description:	
Determination of Amphotericin B levels in ascitic specimens using High Performance Liquid Chromatography	
Reporting group title	Pleural effusion
Reporting group description:	
Determination of Amphotericin B levels in pleural effusion specimens using High Performance Liquid Chromatography	
Reporting group title	Bile
Reporting group description:	
Determination of Amphotericin B levels in bile specimens using High Performance Liquid Chromatography	

Reporting group values	Ascites	Pleural effusion	Bile
Number of subjects	3	7	4
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	2	4	3
From 65-84 years	1	3	1
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	57.67	54.57	58.5
full range (min-max)	44 to 68	29 to 76	50 to 67
Gender categorical Units: Subjects			
Female	0	1	2
Male	3	6	2

Reporting group values	Total		
Number of subjects	14		
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)	9		
From 65-84 years	5		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
full range (min-max)	-		
Gender categorical Units: Subjects			
Female	3		
Male	11		

End points

End points reporting groups

Reporting group title	Ascites
Reporting group description:	
Determination of Amphotericin B levels in ascitic specimens using High Performance Liquid Chromatography	
Reporting group title	Pleural effusion
Reporting group description:	
Determination of Amphotericin B levels in pleural effusion specimens using High Performance Liquid Chromatography	
Reporting group title	Bile
Reporting group description:	
Determination of Amphotericin B levels in bile specimens using High Performance Liquid Chromatography	

Primary: Amphotericin B

End point title	Amphotericin B[1]
End point description:	
Determination of Amphotericin B levels in ascitic, pleural effusion and bile specimens using High Performance Liquid Chromatography	
End point type	Primary
End point timeframe:	
20.07.2007-01-03-2016	

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: Target-site concentration was the primary endpoint of this pharmacokinetic study: In pleural effusion samples, total AMB concentrations were significantly lower than the total concentrations in plasma samples (P = 0.03).

End point values	Ascites	Pleural effusion	Bile	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	7	4	
Units: µg/µL				
arithmetic mean (full range (min-max))	0.31 (0.26 to 0.36)	0.16 (0.02 to 0.43)	0.63 (0.04 to 1.28)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

20.07.2007-01.03.2016

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.03

Reporting groups

Reporting group title	Ascites

Reporting group description:

Determination of Amphotericin B levels in ascitic specimens using High Performance Liquid Chromatography

Reporting group title	Pleural effusion

Reporting group description:

Determination of Amphotericin B levels in pleural effusion specimens using High Performance Liquid Chromatography

Reporting group title	Bile

Reporting group description:

Determination of Amphotericin B levels in bile specimens using High Performance Liquid Chromatography

Serious adverse events	Ascites	Pleural effusion	Bile
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Ascites	Pleural effusion	Bile
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)

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: Drawing blood from an arterial line, which is needed for ICU routine monitoring, is without significant additional risk.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 April 2010	University Hospital for Visceral, Transplant and Thoracic Surgery including ICU was opened for recruitment. Two new subinvestigators were delegated for this trial.
19 February 2014	For assessment of antifungal activity of AmB in patient bile samples, an ex vivo simulation was performed. Assessment was performed at the Institute of Hygiene and Medical Microbiology. Four new subinvestigators were delegated.
28 April 2015	Four ICUs at the Medical University Innsbruck were opened for recruitment. Four new subinvestigators were delegated.

Notes:

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/18662944

http://www.ncbi.nlm.nih.gov/pubmed/17785511

http://www.ncbi.nlm.nih.gov/pubmed/26119497