Clinical trial results:
A Multicenter, Sequential-Panel, Open-Label, Noncomparative Study to Investigate the Safety, Tolerability, and Pharmacokinetics of Caspofungin Acetate in Neonates and Infants Less Than 3 Months of Age

Summary

EudraCT number	2014-005032-34
Trial protocol	Outside EU/EEA
Global end of trial date	06 October 2006

Results information

Result version number	v1 (current)
This version publication date	16 February 2016
First version publication date	17 July 2015

Trial information

Trial identification

Sponsor protocol code	MK-0991-058

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00330395
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000010-PIP01-07
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes
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	06 October 2006
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 October 2006
Global end of trial reached?	Yes
Global end of trial date	06 October 2006
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate plasma concentrations of caspofungin at 1 hour (peak) and 24 hours (trough) after administration of caspofungin 25 mg/m^2 intravenous (IV) to neonates and infants <3 months of age. Safety and tolerability of caspofungin will also be evaluated.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy:

Amphotericin B deoxycholate or a lipid preparation of amphotericin was administered on each day caspofungin was administered. Notably, amphotericin therapy could continue to be administered at the investigator's discretion after caspofungin therapy had ended. After the last day of caspofungin therapy, any additional use of an IV amphotericin B formulation was considered as part of the follow-up period for this study. If the participant was discontinued from IV amphotericin B therapy and not placed on another form of amphotericin or was placed on an azole preparation, the caspofungin therapy was also discontinued.

Evidence for comparator: -

Actual start date of recruitment	24 May 2006
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	Mexico: 4
Country: Number of subjects enrolled	Colombia: 3
Country: Number of subjects enrolled	Panama: 5
Country: Number of subjects enrolled	India: 4
Country: Number of subjects enrolled	United States: 2
Worldwide total number of subjects	18
EEA total number of subjects	0

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	8
Infants and toddlers (28 days-23 months)	10
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The two panels of participants were enrolled sequentially, Panel A followed by Panel B.

Pre-assignment

Screening details:

A total of 21 participants were screened and 18 participants were enrolled.

Period 1

Period 1 title	Overall Study (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	Panel A: Caspofungin Single Dose on Day 1

Arm description:

Participants received caspofungin 25 mg/m^2 in a 1-hour intravenous infusion on Day 1, followed by a 14-day follow-up period.

Arm type	Experimental
Investigational medicinal product name	Caspofungin
Investigational medicinal product code	
Other name	CANCIDAS™, MK-0991
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Caspofungin acetate 25 mg/m^2 in a 1-hour intravenous infusion on Day 1. Infusion employed a pediatric syringe or ambulatory pump.

Arm title	Panel B: Caspofungin Daily for 4 to 28 days

Arm description:

Participants received caspofungin 25 mg/m^2/day in a 1-hour intravenous infusion for a minimum of 4 days and a maximum of 28 days, followed by a 14-day follow-up period.

Arm type	Experimental
Investigational medicinal product name	Caspofungin
Investigational medicinal product code	
Other name	CANCIDAS™, MK-0991
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Caspofungin acetate 25 mg/m^2/day in a 1-hour intravenous infusion for a minimum of 4 days and a maximum of 28 days. Infusion employed a pediatric syringe or ambulatory pump.

Number of subjects in period 1	Panel A: Caspofungin Single Dose on Day 1	Panel B: Caspofungin Daily for 4 to 28 days
Started	6	12
Completed study therapy	6	11
Completed	4	11
Not completed	2	1
Adverse event, serious fatal	2	1

Baseline characteristics

Reporting groups	
Reporting group title	Panel A: Caspofungin Single Dose on Day 1
Reporting group description:	
Participants received caspofungin 25 mg/m^2 in a 1-hour intravenous infusion on Day 1, followed by a 14-day follow-up period.	
Reporting group title	Panel B: Caspofungin Daily for 4 to 28 days
Reporting group description:	
Participants received caspofungin 25 mg/m^2/day in a 1-hour intravenous infusion for a minimum of 4 days and a maximum of 28 days, followed by a 14-day follow-up period.	

Reporting group values	Panel A: Caspofungin Single Dose on Day 1	Panel B: Caspofungin Daily for 4 to 28 days	Total
Number of subjects	6	12	18
Age categorical Units: Subjects			
Age continuous Units: days			
arithmetic mean	3.8	4.9	
standard deviation	± 2.5	± 3.2	-
Gender categorical Units: Subjects			
Female	3	3	6
Male	3	9	12

End points

End points reporting groups

Reporting group title	Panel A: Caspofungin Single Dose on Day 1
Reporting group description:	
Participants received caspofungin 25 mg/m^2 in a 1-hour intravenous infusion on Day 1, followed by a 14-day follow-up period.	
Reporting group title	Panel B: Caspofungin Daily for 4 to 28 days
Reporting group description:	
Participants received caspofungin 25 mg/m^2/day in a 1-hour intravenous infusion for a minimum of 4 days and a maximum of 28 days, followed by a 14-day follow-up period.	
Subject analysis set title	Panel A + Panel B
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants in both panels received caspofungin 25 mg/m^2 in a 1-hour intravenous infusion on Day 1. Participants in Panel B continued to receive caspofungin 25 mg/m^2/day for a minimum of 4 days and a maximum of 28 days. For both panels, the last dose of caspofungin was followed by a 14-day follow-up period.	

Primary: Plasma Concentration of Caspofungin at 24 Hours (C24hr) on Day 1

End point title	Plasma Concentration of Caspofungin at 24 Hours (C24hr) on Day 1[1]
End point description:	
Plasma caspofungin concentrations were measured with a high-performance liquid chromatography method.	
End point type	Primary
End point timeframe:	
Plasma samples for measurement of caspofungin concentrations were collected on Day 1 before dosing and at 1 and 24 hours after initiation of the 1-hour infusion.	
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: Results are displayed for Panels A and B combined; therefore, no statistical analyses were performed for this endpoint.	

End point values	Panel A + Panel B			
Subject group type	Subject analysis set			
Number of subjects analysed	18			
Units: µg/mL				
least squares mean (confidence interval 95%)	1.8 (1.4 to 2.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Caspofungin at One Hour (C1hr) on Day 1

End point title	Plasma Concentration of Caspofungin at One Hour (C1hr) on Day 1
End point description:	
Plasma caspofungin concentrations were measured with a high-performance liquid chromatography	

method.

End point type	Secondary

End point timeframe:

Plasma samples for measurement of caspofungin concentrations were collected on Day 1 before dosing and at 1 and 24 hours after initiation of the 1-hour infusion.

End point values	Panel A + Panel B			
Subject group type	Subject analysis set			
Number of subjects analysed	18			
Units: µg/mL				
least squares mean (confidence interval 95%)	8.2 (6.8 to 10)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Caspofungin at One Hour (C1hr) on Day 4

End point title	Plasma Concentration of Caspofungin at One Hour (C1hr) on Day 4[2]

End point description:

Plasma caspofungin concentrations were measured with a high-performance liquid chromatography method.

End point type	Secondary

End point timeframe:

Plasma samples for measurement of caspofungin concentrations were collected on Day 4 before dosing and at 1 and 24 hours after initiation of the 1-hour infusion.

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint evaluated pharmacokinetics on Day 4. Panel A only collected samples for Day 1 and is not applicable to this endpoint. Therefore only Panel B, which collected samples for Day 4, was evaluated for this endpoint.

End point values	Panel B: Caspofungin Daily for 4 to 28 days			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: µg/mL				
least squares mean (confidence interval 95%)	11.1 (8.8 to 13.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Caspofungin at 24 Hours (C24hr) on Day 4

End point title	Plasma Concentration of Caspofungin at 24 Hours (C24hr) on Day 4[3]

End point description:

Plasma caspofungin concentrations were measured with a high-performance liquid chromatography method.

End point type	Secondary

End point timeframe:

Plasma samples for measurement of caspofungin concentrations were collected on Day 4 before dosing and at 1 and 24 hours after initiation of the 1-hour infusion.

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint evaluated pharmacokinetics on Day 4. Panel A only collected samples for Day 1 and is not applicable to this endpoint. Therefore only Panel B, which collected samples for Day 4, was evaluated for this endpoint.

End point values	Panel B: Caspofungin Daily for 4 to 28 days			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: µg/mL				
least squares mean (confidence interval 95%)	2.4 (1.8 to 3.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with One or More Adverse Events

End point title	Percentage of Participants with One or More Adverse Events

End point description:

An adverse experience is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study drug, whether or not considered related to the use of the product. Any worsening of a preexisting condition which is temporally associated with the use of the product, is also an adverse experience.

End point type	Secondary

End point timeframe:

Up to 14 days after the last dose of study drug.

End point values	Panel A: Caspofungin Single Dose on Day 1	Panel B: Caspofungin Daily for 4 to 28 days		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	12		
Units: Percentage of participants				
number (not applicable)				
Clinical Adverse Events	100	91.7		
Laboratory Adverse Events	0	66.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Discontinued Due to an Adverse Event

End point title	Percentage of Participants Discontinued Due to an Adverse Event

End point description:

An adverse experience is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study drug, whether or not considered related to the use of the product. Any worsening of a preexisting condition which is temporally associated with the use of the product, is also an adverse experience.

End point type	Secondary

End point timeframe:

Up to completion of the last infusion of study drug (Panel A: Day 1; Panel B: up to Day 28)

End point values	Panel A: Caspofungin Single Dose on Day 1	Panel B: Caspofungin Daily for 4 to 28 days		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	12		
Units: Percentage of participants				
number (not applicable)				
Clinical Adverse Event	0	8.3		
Laboratory Adverse Event	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 14 days after the last dose of study drug

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.1

Reporting groups

Reporting group title	Panel A: Caspofungin Single Dose on Day 1

Reporting group description:

Participants received caspofungin 25 mg/m^2 in a 1-hour intravenous infusion on Day 1, followed by a 14-day follow-up period.

Reporting group title	Panel B: Caspofungin Daily for 4 to 28 days

Reporting group description:

Participants received caspofungin 25 mg/m^2/day in a 1-hour intravenous infusion for a minimum of 4 days and a maximum of 28 days, followed by a 14-day follow-up period.

Serious adverse events	Panel A: Caspofungin Single Dose on Day 1	Panel B: Caspofungin Daily for 4 to 28 days	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 6 (33.33%)	3 / 12 (25.00%)	
number of deaths (all causes)	2	1	
number of deaths resulting from adverse events			
Congenital, familial and genetic disorders			
Patent ductus arteriosus			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Nervous system disorders			
Hypoxic encephalopathy			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Intestinal perforation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Intestinal stenosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising colitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Infections and infestations			
Bacterial sepsis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter sepsis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			

subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Fungal endocarditis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

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

Non-serious adverse events	Panel A: Caspofungin Single Dose on Day 1	Panel B: Caspofungin Daily for 4 to 28 days	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)	11 / 12 (91.67%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Band neutrophil count increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Bilirubin conjugated increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 6 (0.00%)	3 / 12 (25.00%)	
occurrences (all)	0	6	
Blood bilirubin increased			

subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)		
occurrences (all)	0	1		
Blood cholesterol increased				
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)		
occurrences (all)	0	4		
Blood creatinine increased				
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)		
occurrences (all)	0	1		
Blood glucose increased				
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)		
occurrences (all)	0	1		
Blood lactate dehydrogenase increased				
subjects affected / exposed	0 / 6 (0.00%)	3 / 12 (25.00%)		
occurrences (all)	0	6		
Blood potassium decreased				
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)		
occurrences (all)	0	1		
Blood potassium increased				
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)		
occurrences (all)	0	1		
Blood triglycerides increased				
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)		
occurrences (all)	0	4		
Blood urea increased				
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)		
occurrences (all)	0	2		
C-reactive protein increased				
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)		
occurrences (all)	0	1		
Gamma-glutamyltransferase increased				
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)		
occurrences (all)	0	5		
Haematocrit decreased				

subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Haemoglobin decreased			
subjects affected / exposed	0 / 6 (0.00%)	3 / 12 (25.00%)	
occurrences (all)	0	4	
Neutrophil count increased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	3	
Oxygen saturation decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	2	
Platelet count decreased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
White blood cell count increased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	3	
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	1 / 6 (16.67%)	2 / 12 (16.67%)	
occurrences (all)	1	6	
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Sinus tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	6	
Nervous system disorders			

Cerebral atrophy			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Intraventricular haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Anaemia neonatal			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Hypothermia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	3 / 12 (25.00%)	
occurrences (all)	0	9	
Eye disorders			
Retinopathy of prematurity			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Anal fissure			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Haematochezia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Perianal erythema			

subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
Apnoeic attack			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Bronchopulmonary dysplasia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Chronic respiratory disease			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Hyperventilation			
subjects affected / exposed	0 / 6 (0.00%)	3 / 12 (25.00%)	
occurrences (all)	0	11	
Pulmonary congestion			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Respiratory distress			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Infections and infestations			
Conjunctivitis bacterial			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Enterobacter sepsis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Sepsis neonatal			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			

Fluid overload			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Hypoglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Malnutrition			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	

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