Clinical trial results:
A multicenter, open-label, single-arm, multiple-dose study to evaluate the safety, pharmacokinetics, and efficacy of ceftobiprole medocaril in term and pre-term neonates and infants up to 3 months of age with late-onset sepsis

Summary

EudraCT number	2022-001837-35
Trial protocol	LT LV SK PL Outside EU/EEA EE BG DE
Global end of trial date	18 December 2024

Results information

Result version number	v1 (current)
This version publication date	02 July 2025
First version publication date	02 July 2025

Trial information

Trial identification

Sponsor protocol code	BPR-PIP-003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05856227
WHO universal trial number (UTN)	-
Other trial identifiers	IND Number: 64.407

Notes:

Sponsors

Sponsor organisation name	Basilea Pharmaceutica International Ltd, Allschwil
Sponsor organisation address	Hegenheimermattweg 167b, Allschwil, Switzerland, 4123
Public contact	Study director, Basilea Pharmaceutica International Ltd, Allschwil, +41 616061111, medical.information@basilea.com
Scientific contact	Study director, Basilea Pharmaceutica International Ltd, Allschwil, +41 616061111, medical.information@basilea.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000205-PIP02-11
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 February 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 December 2024
Global end of trial reached?	Yes
Global end of trial date	18 December 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To characterise the safety profile of ceftobiprole in term and pre-term neonates and infants up to 3 months of age with LOS.

Protection of trial subjects:

The study was conducted according to the ethical principles that have their origins in the World Medical Association Declaration of Helsinki, the International Council for Harmonisation (ICH) E6 Good Clinical Practice (GCP), and applicable national and local laws and regulations for the conduct of clinical research and the protection of personal data. If conflicts between local laws and regulations arose, more stringent requirements were adopted.

Background therapy:

The investigational medicinal product, ceftobiprole may have been combined with locally-provided ampicillin and/or an aminoglycoside based on the Investigator’s judgment.

Evidence for comparator:

Not applicable

Actual start date of recruitment	06 August 2023
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	Bulgaria: 3
Country: Number of subjects enrolled	Estonia: 2
Country: Number of subjects enrolled	Lithuania: 1
Country: Number of subjects enrolled	United States: 2
Worldwide total number of subjects	9
EEA total number of subjects	7

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	6
Newborns (0-27 days)	2

Infants and toddlers (28 days-23 months)	1
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:

Recruitment began in August 2023. The study included pediatric patients from Europe and the USA.

Pre-assignment

Screening details:

A total of 11 patients were screened for enrollment in this study, two of whom failed the screening process. Nine patients (six pre-term neonates and three term neonates) were enrolled and assigned to the study treatment.

Period 1

Period 1 title	Overall Trial (ITT/Safety population) (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	Pre-term Neonates

Arm description:

Pediatric patients (gestational age ≥ 24 to 36 weeks), with post-natal age ranging from ≥ 3 days to ≤ 3 months.
Patients were treated with ceftobiprole 7.5 mg/kg or 10 mg/kg (bodyweight < 4 kg) infused over 2 hours and administered every 12 hours.
Ceftobiprole may have been combined with locally-provided ampicillin and/or an aminoglycoside based on the Investigator’s judgment.

Arm type	Experimental
Investigational medicinal product name	Ceftobiprole medocaril
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Study treatment consisted of IV ceftobiprole medocaril for 3 – 10 days, which could be extended to 14 days if considered clinically necessary by the Investigator. Ceftobiprole was administered as a 2-hour IV infusion, with the dose adjusted according to gestational and post-natal ages. To limit infusion volume for the pre-term and term neonates, the ceftobiprole medocaril infusion was administered at a concentration of 4 mg/mL.

Arm title	Term Neonates

Arm description:

Pediatric patients (gestational age ≥ 37 weeks), with post-natal age ranging from ≥ 3 days to ≤ 3 months.
Patients were treated with ceftobiprole 10 mg/kg (bodyweight < 4 kg) or 15mg/kg (bodyweight ≥ 4 kg) infused over 2 hours and administered every 12 hours.
Ceftobiprole may have been combined with locally-provided ampicillin and/or an aminoglycoside based on the Investigator’s judgment

Arm type	Experimental
Investigational medicinal product name	Ceftobiprole medocaril
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Study treatment consisted of IV ceftobiprole medocaril for 3 – 10 days, which could be extended to 14 days if considered clinically necessary by the Investigator. Ceftobiprole was administered as a 2-hour IV infusion, with the dose adjusted according to gestational and post-natal ages. To limit infusion volume for the pre-term and term neonates, the ceftobiprole medocaril infusion was administered at a concentration of 4 mg/mL.

Number of subjects in period 1	Pre-term Neonates	Term Neonates
Started	6	3
Completed	4	2
Not completed	2	1
Adverse event, non-fatal	-	1
Due to Investigator absence	1	-
Cerebrospinal fluid test positive for S. aureus	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Pre-term Neonates
Reporting group description:	
Pediatric patients (gestational age ≥ 24 to 36 weeks), with post-natal age ranging from ≥ 3 days to ≤ 3 months. Patients were treated with ceftobiprole 7.5 mg/kg or 10 mg/kg (bodyweight < 4 kg) infused over 2 hours and administered every 12 hours. Ceftobiprole may have been combined with locally-provided ampicillin and/or an aminoglycoside based on the Investigator's judgment.	
Reporting group title	Term Neonates
Reporting group description:	
Pediatric patients (gestational age ≥ 37 weeks), with post-natal age ranging from ≥ 3 days to ≤ 3 months. Patients were treated with ceftobiprole 10 mg/kg (bodyweight < 4 kg) or 15mg/kg (bodyweight ≥ 4 kg) infused over 2 hours and administered every 12 hours. Ceftobiprole may have been combined with locally-provided ampicillin and/or an aminoglycoside based on the Investigator's judgment	

Reporting group values	Pre-term Neonates	Term Neonates	Total
Number of subjects	6	3	9
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	6	0	6
Newborns (0-27 days)	0	2	2
Infants and toddlers (28 days-23 months)	0	1	1
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: days			
arithmetic mean	19.2	26.7	
standard deviation	± 11.05	± 4.51	-
Gender categorical Units: Subjects			
Female	3	1	4
Male	3	2	5
Race Units: Subjects			
White	5	3	8
Unknown or Not Reported	1	0	1
Gestational age Units: Weeks			
arithmetic mean	28.5	39.0	
standard deviation	± 4.68	± 1.73	-
Baseline weight			

Units: gram(s)			
arithmetic mean	1429.2	3156.7	
standard deviation	± 777.49	± 1094.36	-

End points

End points reporting groups

Reporting group title	Pre-term Neonates

Reporting group description:

Pediatric patients (gestational age ≥ 24 to 36 weeks), with post-natal age ranging from ≥ 3 days to ≤ 3 months.
Patients were treated with ceftobiprole 7.5 mg/kg or 10 mg/kg (bodyweight < 4 kg) infused over 2 hours and administered every 12 hours.
Ceftobiprole may have been combined with locally-provided ampicillin and/or an aminoglycoside based on the Investigator's judgment.

Reporting group title	Term Neonates

Reporting group description:

Pediatric patients (gestational age ≥ 37 weeks), with post-natal age ranging from ≥ 3 days to ≤ 3 months.
Patients were treated with ceftobiprole 10 mg/kg (bodyweight < 4 kg) or 15mg/kg (bodyweight ≥ 4 kg) infused over 2 hours and administered every 12 hours.
Ceftobiprole may have been combined with locally-provided ampicillin and/or an aminoglycoside based on the Investigator's judgment

Primary: Number of Patients With Adverse Events (AEs)

End point title	Number of Patients With Adverse Events (AEs)[1]

End point description:

Number of patients with AEs, serious adverse events (SAEs), AEs leading to discontinuations and AEs of special interest

End point type	Primary

End point timeframe:

Up to 5–7 weeks

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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Pre-term Neonates	Term Neonates		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	3		
Units: Count of Participants				
number (not applicable)				
Any AE	3	3		
Study-drug-related AE	0	0		
SAE	1	1		
Study-drug-related SAE	0	0		
AE leading to treatment discontinuation	0	1		
AE of special interest	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of Ceftobiprole, Ceftobiprole Medocaril, and Open-ring Metabolite

End point title	Maximum Observed Plasma Concentration (Cmax) of Ceftobiprole, Ceftobiprole Medocaril, and Open-ring Metabolite

End point description:

Observed pharmacokinetic parameter Cmax of ceftobiprole (the active moiety), its pro-drug ceftobiprole medocaril and the open-ring metabolite in term and pre-term neonates with post-natal age up to 3 months

End point type	Secondary

End point timeframe:

On treatment Day 3 prior to and 2, 4, and 8 hours after the start of the first ceftobiprole infusion of the day.

End point values	Pre-term Neonates	Term Neonates		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	3		
Units: µg/mL				
median (full range (min-max))				
Ceftobiprole	17.2 (11.0 to 22.6)	28.4 (19.1 to 33.8)		
Ceftobiprole medocaril	0.585 (0.276 to 5.70)	0.552 (0.376 to 2.59)		
Open-ring metabolite	1.18 (0.624 to 1.69)	1.68 (0.998 to 2.06)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Improved Signs and Symptoms of Late Onset Sepsis (LOS)

End point title	Number of Participants With Improved Signs and Symptoms of Late Onset Sepsis (LOS)

End point description:

Improved signs and symptoms of LOS (including fever, hypothermia, abnormal heart rate, signs of impaired circulation, petechial rash or sclerema neonatorum, respiratory distress, gastrointestinal distress, irritability, lethargy and/or muscular or arterial hypotonia) assessed at Day 3, EOT, and TOC visits (ITT) populations.

End point type	Secondary

End point timeframe:

At the Day 3 and up to 5-7 weeks

End point values	Pre-term Neonates	Term Neonates		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	3		
Units: Number of Patients				
number (not applicable)				
Day 3 Resolved	1	1		
Day 3 Improved	1	0		
Day 3 Unchanged	3	1		
Day 3 Worsened	0	1		
Day 3 Not done	1	0		
EoT Resolved	1	1		
EoT Improved	1	0		
EoT unchanged	2	1		
EoT Worsened	1	0		
EoT Not done	1	1		
TOC Resolved	2	2		
TOC Improved	2	0		
TOC unchanged	1	0		
TOC Worsened	1	1		
TOC Not done	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients With a Clinical Response

End point title	Number of Patients With a Clinical Response
End point description:	
Clinical cure rate at the end of treatment (EOT) at day 3-14 and test of cure (TOC) at 7–14 days after last ceftobiprole dose visits in the Intent-to-Treat (ITT) population	
End point type	Secondary
End point timeframe:	
5-7 weeks	

End point values	Pre-term Neonates	Term Neonates		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	3		
Units: Number of Participants				
number (not applicable)				
EOT Cure	4	2		
EoT Failure	0	1		
EoT Unevaluable	2	0		
TOC Cure	4	2		
TOC Failure	0	1		
TOC Unevaluable	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients With a Microbiological Response

End point title	Number of Patients With a Microbiological Response

End point description:

Microbiological eradication or presumed eradication rate at the EOT and TOC visits.

End point type	Secondary

End point timeframe:

5-7 weeks

End point values	Pre-term Neonates	Term Neonates		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	3		
Units: Number of Participants				
number (not applicable)				
EOT Eradication	4	1		
EOT Presumed eradication	0	1		
EOT Persistence	0	1		
EOT Unevaluable	2	0		
TOC Eradication	4	1		
TOC Presumed eradication	0	1		
TOC Persistence	0	1		
TOC Unevaluable	2	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first administration of study medication up to LFU visit.	
Adverse event reporting additional description:	
Treatment-emergent adverse events and serious adverse events	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups	
Reporting group title	Term Neonates
Reporting group description:	
Term neonates	
Reporting group title	Pre-term neonates
Reporting group description:	
Pre-term neonates	

Serious adverse events	Term Neonates	Pre-term neonates	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Enterobacter sepsis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Term Neonates	Pre-term neonates	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 6 (50.00%)	
Investigations			
Haemoglobin decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Vena cava thrombosis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Intraventricular haemorrhage neonatal			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	2	
Thrombocytosis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Oedema			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	
occurrences (all)	0	4	
Withdrawal syndrome			

subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 6 (0.00%) 0	
Gastrointestinal disorders Gastrointestinal haemorrhage subjects affected / exposed occurrences (all)	 1 / 3 (33.33%) 1	 0 / 6 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Bronchopulmonary dysplasia subjects affected / exposed occurrences (all)	 0 / 3 (0.00%) 0	 1 / 6 (16.67%) 1	
Endocrine disorders Adrenal haemorrhage subjects affected / exposed occurrences (all)	 1 / 3 (33.33%) 1	 0 / 6 (0.00%) 0	
Infections and infestations Osteomyelitis subjects affected / exposed occurrences (all) Sepsis neonatal subjects affected / exposed occurrences (all)	 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0	 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1	
Metabolism and nutrition disorders Hypoglycaemia subjects affected / exposed occurrences (all) Hyponatraemia subjects affected / exposed occurrences (all)	 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0	 1 / 6 (16.67%) 3 1 / 6 (16.67%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 July 2024	The number of term and pre-term neonates was reduced from at least 15 to at least 8 patients, comprising at least two term neonates, and at least six pre-term neonates less than < 37 weeks gestational age.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported