

BOLOGNA
& ONLINE
1-5 JUNE
2026



Open-Label Phase 2 Study of Single and Multiple Doses of Cefiderocol in Hospitalised Infants Aged Less than 3 Months with Suspected/Confirmed Aerobic Gram-negative Bacterial Infections

44TH ANNUAL MEETING OF THE
EUROPEAN SOCIETY FOR
PAEDIATRIC INFECTIOUS DISEASES
Organised jointly by ESPID and the ESPID Foundation

#ESPID2026
espidmeeting.org

Conflict of Interest

	No, Nothing to disclose
X	Yes, please specify

Company / Name	Honoraria / Expense	Consulting / Advisory Board	Funded Research	Royalties / Patent	Stock Options	Ownership / Equity Position	Employee	Other (Please specify)
Shionogi / Jesus Gonzalez							Yes	
Shionogi / Oluwaseun Makinde							Yes	
Shionogi / Simon Portsmouth							Yes	
Shionogi / Aarifah Bijabhai							Yes	
Shionogi / Mari Ariyasu							Yes	
Shionogi / Takamichi Baba							Yes	
Shionogi / Takayuki Katsube							Yes	

Conflict of Interest

X	No, Nothing to disclose
	Yes, please specify

Company / Name	Honoraria / Expense	Consulting / Advisory Board	Funded Research	Royalties / Patent	Stock Options	Ownership / Equity Position	Employee	Other (Please specify)
Adrie Bekker								
Sithembiso Velaphi								
Tanusha Ramdin								
Phuc Huu Phan								

Open-Label Phase 2 Study of Single and Multiple Doses of Cefiderocol in Hospitalised Infants Aged Less than 3 Months with Suspected/Confirmed Aerobic Gram-negative Bacterial Infections

Jesus Gonzalez,[1] Adrie Bekker,[2] Tanusha Ramdin,[3] Sithembiso Velaphi,[4] Phuc Huu Phan,[5] Simon Portsmouth,[6] Aarifah Bijabhai,[1] Mari Ariyasu,[7] Takamichi Baba,[7] Takayuki Katsube,[7] Oluwaseun Makinde[6]

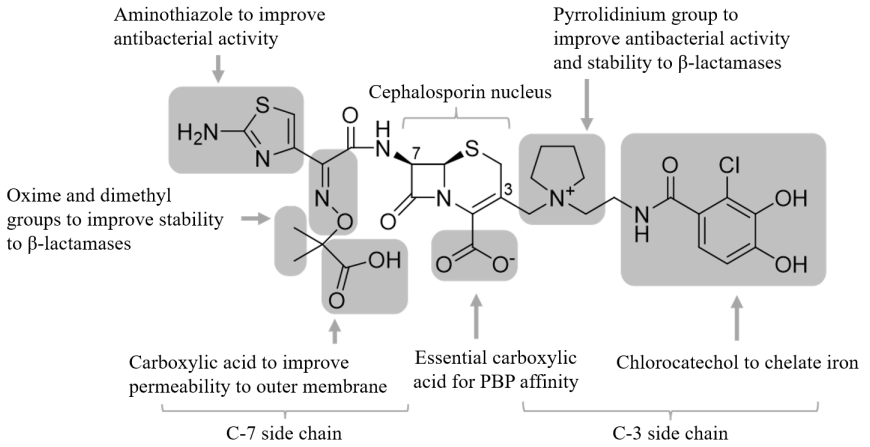
[1]Shionogi B.V., London, UK; [2]Department of Paediatrics and Child Health, Stellenbosch University, Cape Town, South Africa; [3]Department of Paediatric and Child Health, Charlotte Maxeke Johannesburg Academic Hospital, University of the Witwatersrand, Johannesburg, South Africa; [4]Department of Paediatrics and Child Health, Chris Hani Baragwanath Academic Hospital, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa; [5]Vietnam National Children's Hospital, Hanoi, Vietnam; [6]Shionogi Inc., Florham Park, NJ, USA; [7]Shionogi & Co., Ltd., Osaka, Japan.

NCT06086626
Funding: the study was funded by Shionogi & Co., Ltd., Osaka, Japan.

Introduction

- Serious Gram-negative bacterial infections are associated with increased morbidity and mortality in neonates and infants in regions with high burden of antimicrobial resistance[1]
- Antibiotics showing safety and efficacy are needed for this age group[2]
  - ✓ Cefiderocol is a siderophore cephalosporin with *in vitro* activity against aerobic Gram-negative bacteria[3]
  - ✓ Cefiderocol paediatric clinical development programme included a Phase 2 study enrolling neonates and young infants

Cefiderocol[4]



Approved indications in adults[5,6]

- FDA: Complicated urinary tract infection, hospital-acquired and ventilator-associated bacterial pneumonia
- EMA: Gram-negative bacterial infections with limited treatment options

EMA, European Medicines Agency; FDA, US Food and Drug Administration; PBP, penicillin-binding protein.

1. Russell NJ, et al. PLoS Med. 2023;20(6):e1004179; 2. Van den Anker JN, et al. Pharmaceutics. 2020;12(7):685; 3. Bianco G, et al. Curr Issues Mol Biol. 2024;46(12):14132–14153; 4. Sato T, et al. Clin Infect Dis. 2019;69 (Suppl 7):S538–S543; 5. Fetroja (cefiderocol). Prescribing Information. Shionogi Inc., USA, 2026; 6. Fetcroja (cefiderocol). Summary of Product Characteristics. Shionogi B.V., The Netherlands, 2025.

Study Design and Objectives

- **NEO-CEFI study**: A non-randomised, multicentre, open-label, Phase 2 study

- **Objectives**: To assess the pharmacokinetics, safety and tolerability of cefiderocol after single-dose and multiple-dose administration

- **Target population**: Hospitalised patients from birth to <3 months of age with suspected or confirmed aerobic Gram-negative bacterial infections, including urinary tract infections, intra-abdominal infections, hospital-acquired or ventilator-associated bacterial pneumonia, and bloodstream infection or sepsis, who were expected to be treated with systemic standard-of-care antibiotics for approximately 5–14 days

Patient Age Cohorts

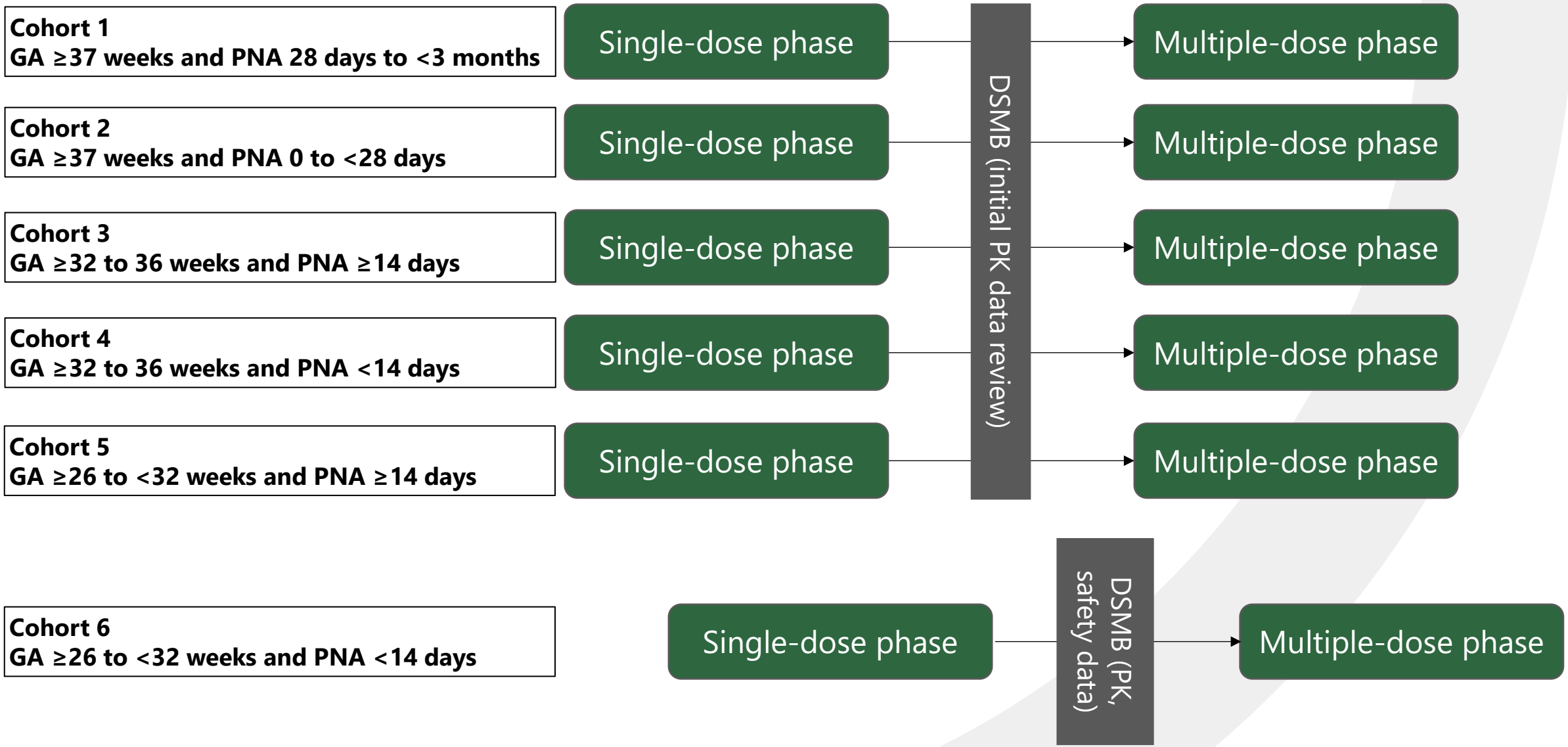
- Neonates were enrolled into 6 age cohorts based on gestational age (GA) and postnatal age (PNA):
    1. GA ≥37 weeks and PNA 28 days to <3 months
    2. GA ≥37 weeks and PNA 0 to <28 days
    3. GA ≥32 to 36 weeks and PNA ≥14 days
    4. GA ≥32 to 36 weeks and PNA <14 days
    5. GA ≥26 to <32 weeks and PNA ≥14 days
    6. GA ≥26 to <32 weeks and PNA <14 days

- Written informed consent was provided for all eligible patients by their parents or legally authorised guardians

Key Exclusion Criteria

- Patients who met any of the following criteria were excluded from the study:
  - History of hypersensitivity or allergic reaction to any beta-lactam antibiotic
  - Confirmed Gram-positive bacteria, or viral infection, or fungal infection, or parasitic pathogen
  - Confirmed Gram-negative bacteria resistant to cefiderocol
  - Suspected or confirmed central nervous system infection
  - Urine output <1 mL/kg/hour within 24 hours prior to administration of study drug on Day 1

Study Schematic



DSMB, Data Safety Monitoring Board; GA, gestational age; PK, pharmacokinetics; PNA, postnatal age.

Cefiderocol Dosing

Postnatal age	Frequency of infusion in multiple-dose phase	Dose per infusion	
		Gestational age ≥32 weeks	Gestational age <32 weeks
Birth to <2 months	Every 8 hours	40 mg/kg	30 mg/kg
2–<3 months	Every 8 hours	60 mg/kg	40 mg/kg

1. **Single-dose phase:** all patients received cefiderocol as a single **3-hour infusion**

2. **Multiple-dose phase:** patients received cefiderocol as **3-hour** or **1-hour infusions** every 8 hours for a recommended duration of at least 5 days

SOC dosing regimens were selected at the discretion of the investigator, consistent with prescribing information and in accordance with local standards

 SOC, standard-of-care.

Demographic Characteristics in the Single-Dose Phase (Safety Population)

	Single-dose phase						
	C1 N=1	C2 N=2	C3 N=3	C4 N=0	C5 N=3	C6 N=3	**Overall N=12**
GA (weeks)							
Median	38.1	40.7	34.7	0	28.3	31.0	**31.5**
Min, max	38, 38	40, 41	32, 36	0	26, 30	29, 31	**26, 41**
PNA (days)							
Median	33.0	9.0	30.0	0	59.0	10.0	**16.5**
Min, max	33, 33	5, 13	16, 34	0	17, 60	4, 13	**4, 60**
Sex, n (%)							
Male	1 (100)	2 (100)	3 (100)	0	1 (33.3)	0	**7 (58.3)**
Female	0	0	0	0	2 (66.7)	3 (100)	**5 (41.7)**
Race, n (%)							
White	0	0	1 (33.3)	0	0	0	**1 (8.3)**
Black/African-American	0	1 (50.0)	1 (33.3)	0	3 (100)	3 (100)	**8 (66.7)**
Asian	1 (100)	0	1 (33.3)	0	0	0	**2 (16.7)**
Other	0	1 (50.0)	0	0	0	0	**1 (8.3)**
Ethnicity, n (%)							
Hispanic/Latino	0	0	0	0	0	0	**0**
Body weight (kg)							
Median	4.48	3.05	2.7	0	1.3	1.36	**1.95**
Min, max	4.48, 4.48	3.00, 3.10	1.90, 2.85	0	1.10, 2.00	1.00, 1.50	**1.00, 4.48**
Infection type, n (%)							
BSI	0	0	0	0	0	0	**0**
Sepsis	0	0	1 (33.3)	0	0	1 (33.3)	**2 (16.7)**
IAI	0	1 (50.0)	0	0	3 (100)	2 (66.7)	**6 (50.0)**
UTI	1 (100)	0	1 (33.3)	0	0	0	**2 (16.7)**
Pneumonia	0	1 (50.0)	1 (33.3)	0	0	0	**2 (16.7)**
Other	0	0	0	0	0	0	**0**

- There were no patients in Cohort 4
- Mostly Black/African-American patients
- Mostly IAI; however, infection type varied by cohort

C1: GA ≥37 weeks and PNA 28 days to <3 months; C2: GA ≥37 weeks and PNA 0 to <28 days; C3: GA ≥32 to 36 weeks and PNA ≥14 days; C4: GA ≥32 to 36 weeks and PNA <14 days; C5: GA ≥26 to <32 weeks and PNA ≥14 days; C6: GA ≥26 to <32 weeks and PNA <14 days.
BSI, bloodstream infection; C, cohort; GA, gestational age; IAI, intra-abdominal infection; PNA, postnatal age; UTI, urinary tract infection.

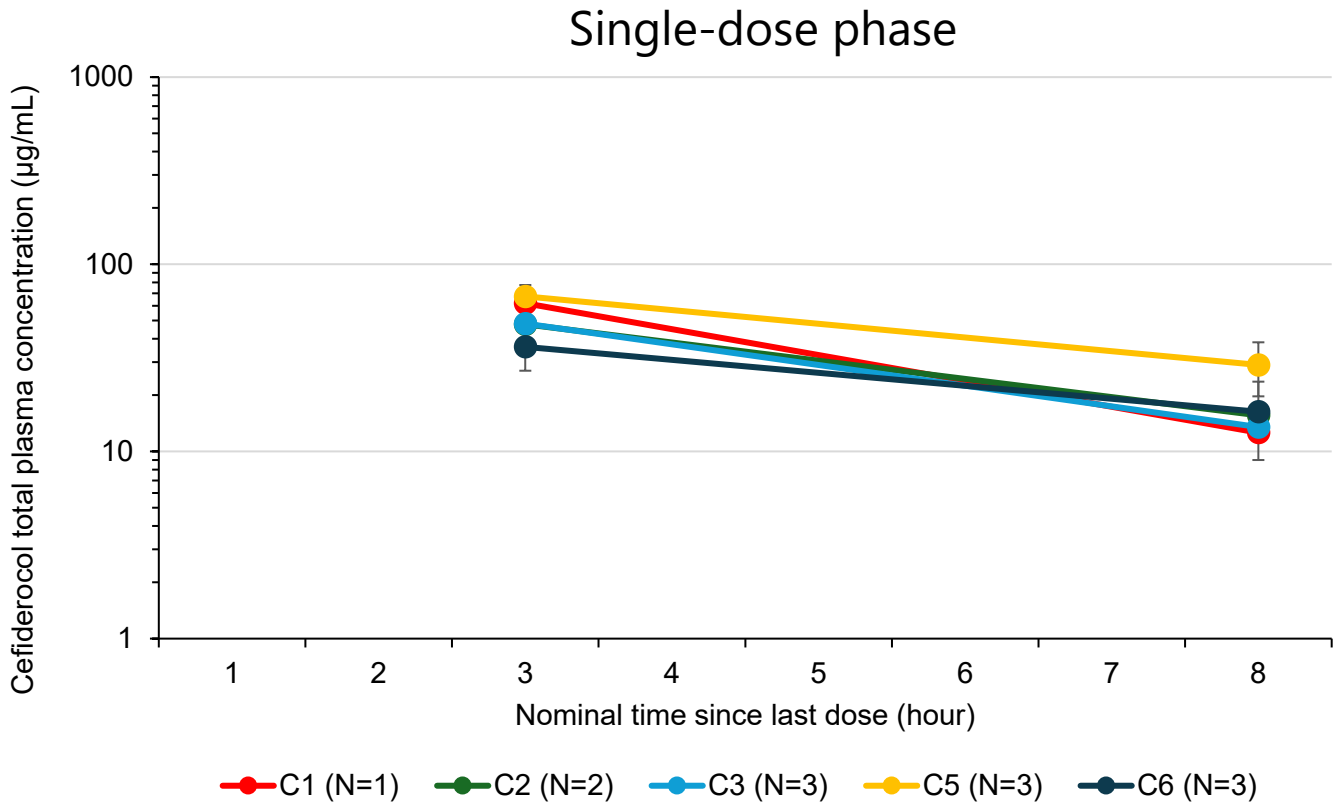
Demographic Characteristics in the Multiple-Dose Phase (Safety Population)

	Multiple-dose phase						
	C1 N=0	C2 N=6	C3 N=1	C4 N=5	C5 N=2	C6 N=4	**Overall N=18**
GA (weeks)							
Median	0	40.4	35.0	33.0	29.5	28.8	**33.0**
Min, max	0	37, 41	35, 35	32, 35	28, 31	28, 31	**28, 41**
PNA (days)							
Median	0	3.5	25.0	5.0	19.0	7.0	**5.5**
Min, max	0	2, 19	25, 25	2, 7	17, 21	4, 12	**2, 25**
Sex, n (%)							
Male	0	3 (50.0)	1 (100)	1 (20.0)	2 (100)	2 (50.0)	**9 (50.0)**
Female	0	3 (50.0)	0	4 (80.0)	0	2 (50.0)	**9 (50.0)**
Race, n (%)							
White	0	1 (16.7)	0	0	0	0	**1 (5.6)**
Black/African-American	0	2 (33.3)	1 (100)	3 (60.0)	2 (100)	2 (50.0)	**10 (55.6)**
Asian	0	2 (33.3)	0	1 (20.0)	0	2 (50.0)	**5 (27.8)**
Other	0	1 (16.7)	0	1 (20.0)	0	0	**2 (11.1)**
Ethnicity, n (%)							
Hispanic/Latino	0	0	0	1 (20.0)	0	0	**1 (5.6)**
Body weight (kg)							
Median	0	3.25	1.53	1.69	1.27	1.12	**1.68**
Min, max	0	2.54, 3.82	1.53, 1.53	1.59, 2.19	1.10, 1.45	1.10, 1.50	**1.10, 3.82**
Infection type, n (%)							
BSI	0	0	0	2 (40.0)	0	1 (25.0)	**3 (16.7)**
Sepsis	0	2 (33.3)	1 (100)	1 (20.0)	0	2 (50.0)	**6 (33.3)**
IAI	0	0	0	0	1 (50.0)	0	**1 (5.6)**
UTI	0	0	0	0	0	0	**0**
Pneumonia	0	3 (50.0)	0	2 (40.0)	1 (50.0)	1 (25.0)	**7 (38.9)**
Other[a]	0	1 (16.7)	0	0	0	0	**1 (5.6)**

- There were no patients in Cohort 1
- Mostly Black/African-American patients
- Mostly pneumonia and sepsis
- BSI and IAI mainly in Cohorts 4 and 5

C1: GA ≥37 weeks and PNA 28 days to <3 months; C2: GA ≥37 weeks and PNA 0 to <28 days; C3: GA ≥32 to 36 weeks and PNA ≥14 days; C4: GA ≥32 to 36 weeks and PNA <14 days; C5: GA ≥26 to <32 weeks and PNA ≥14 days; C6: GA ≥26 to <32 weeks and PNA <14 days.
[a]Gastrointestinal infection (n=1).
BSI, bloodstream infection; C, cohort; GA, gestational age; IAI, intra-abdominal infection; PNA, postnatal age; UTI, urinary tract infection.

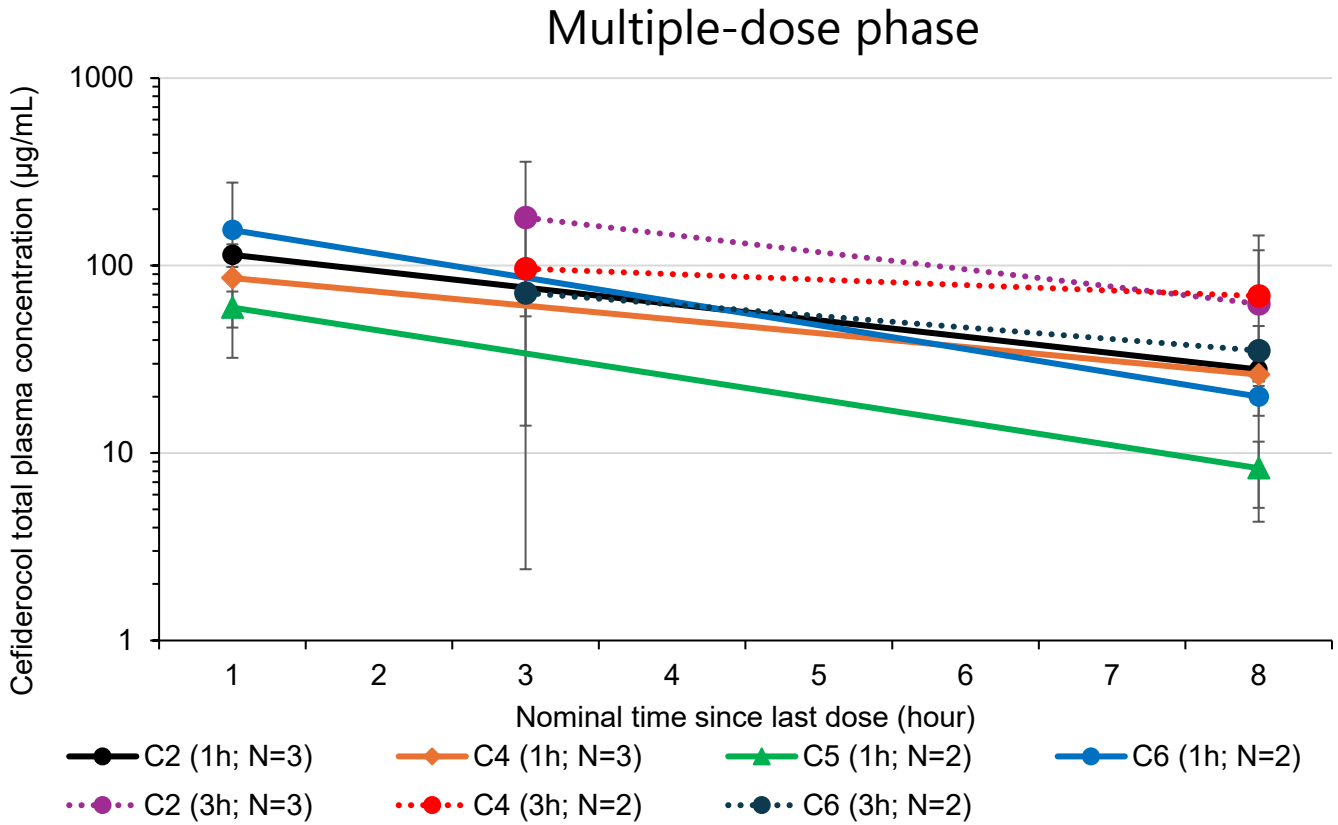
Cefiderocol Total Plasma Concentrations After a Single 3-hour Infusion



- Geometric mean concentrations:
  - C_{max} at the end of infusion: 35.5–66.9 µg/mL
  - C_{min} at the end of the dosing period: 12.6–28.2 µg/mL

C1: GA ≥37 weeks and PNA 28 days to <3 months; C2: GA ≥37 weeks and PNA 0 to <28 days; C3: GA ≥32 to 36 weeks and PNA ≥14 days; C5: GA ≥26 to <32 weeks and PNA ≥14 days; C6: GA ≥26 to <32 weeks and PNA <14 days.
C, cohort; CLSI, Clinical and Laboratory Standards Institute; C_{max}, maximum concentration; C_{min}, minimum concentration; EUCAST, European Committee on Antimicrobial Susceptibility Testing.
Data are shown as arithmetic mean (standard deviation). Cefiderocol unbound fraction: 0.422 (Katsube T, et al. *J Antimicrob Chemother* 2019; 74: 1971-4).

Cefiderocol Total Plasma Concentrations with 1-hour or 3-hour Infusions



- Geometric mean concentrations:
  - C_{max} at the end of infusion: 59.0–128.2 µg/mL (1 hour); 70.3–129.1 µg/mL (3 hours)
  - C_{min} at the end of the dosing period: 8.0–27.7 µg/mL (1 hour); 34.1–47.0 µg/mL (3 hours)
  - Median exposure: 3.0–7.0 days across age cohorts

C2: GA ≥37 weeks and PNA 0 to <28 days; C4: GA ≥32 to 36 weeks and PNA <14 days; C5: GA ≥26 to <32 weeks and PNA ≥14 days; C6: GA ≥26 to <32 weeks and PNA <14 days.
C, cohort; CLSI, Clinical and Laboratory Standards Institute; C_{max}, maximum concentration; C_{min}, minimum concentration; EUCAST, European Committee on Antimicrobial Susceptibility Testing.
Data are shown as arithmetic mean (standard deviation). Cefiderocol unbound fraction: 0.422 (Katsube T, et al. *J Antimicrob Chemother* 2019; 74: 1971-4).

Treatment-Emergent Adverse Events – Overall Summary (Safety Population)

	Single-dose phase							Multiple-dose phase						
	C1 N=1	C2 N=2	C3 N=3	C4 N=0	C5 N=3	C6 N=3	**Overall N=12**	C1 N=0	C2 N=6	C3 N=1	C4 N=5	C5 N=2	C6 N=4	**Overall N=18**
Any TEAEs, n (%)	1 (100)	1 (50.0)	1 (33.3)	0	2 (66.7)	0	**5 (41.7)**	0	6 (100)	1 (100)	3 (60.0)	2 (100)	4 (100)	**16 (88.9)**
Any serious TEAEs	0	0	0	0	2 (66.7)[a]	0	**2 (16.7)**	0	3 (50.0)[b]	0	0	1 (50.0)[e]	1 (25.0)[f]	**5 (27.8)**
Non-fatal SAEs	0	0	0	0	1 (33.3)[a]	0	**1 (8.3)**	0	3 (50.0)[b]	0	0	1 (50.0)[e]	1 (25.0)[f]	**5 (27.8)**
Any treatment-related TEAEs	0	0	0	0	0	0	**0**	0	1 (16.7)[c]	0	1 (20.0)[d]	0	0	**2 (11.1)**
Any treatment-related SAEs	0	0	0	0	0	0	**0**	0	0	0	0	0	0	**0**
Any TEAE leading to discontinuation	0	0	0	0	0	0	**0**	0	0	0	0	0	1 (25.0)[g]	**1 (5.6)**
Any TEAE leading to death	0	0	0	0	1 (33.3)[a]	0	**1 (8.3)**	0	0	0	0	0	0	**0**

[a]Two patients and three serious adverse events; non-fatal necrotising enterocolitis in 1 patient, resolved; multiorgan dysfunction syndrome and sepsis leading to death in 1 patient.
[b]One patient experienced life-threatening neonatal sepsis, one patient experienced mild subcutaneous abscess, one patient experienced moderate diarrhoea (all resolved).
[c]Oral candidiasis (related, recovered).
[d]Moderate leukopenia (related, recovered).
[e]One patient experienced life-threatening small-intestine perforation (unrelated, resolved).
[f]One patient experienced moderate vascular device infection (unrelated, resolved).
[g]Candida infection leading to cefiderocol discontinuation (unrelated, resolved).
A TEAE is an adverse event with onset after the first dose of study intervention. Adverse Events were coded using Medical Dictionary for Regulatory Activities (MedDRA), Version 26.0.

No safety concerns were identified

C1: GA ≥37 weeks and PNA 28 days to <3 months; C2: GA ≥37 weeks and PNA 0 to <28 days; C3: GA ≥32 to 36 weeks and PNA ≥14 days; C4: GA ≥32 to 36 weeks and PNA <14 days; C5: GA ≥26 to <32 weeks and PNA ≥14 days; C6: GA ≥26 to <32 weeks and PNA <14 days.
C, cohort; GA, gestational age; PNA, postnatal age; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Conclusions

- Total maximum plasma concentrations of cefiderocol were similar between single-dose phase and multiple-dose phase regardless of the infusion duration and without drug accumulation
- Both total and calculated unbound trough concentrations of cefiderocol remained above the CLSI and EUCAST susceptibility breakpoints for Gram-negative bacteria for the entire dosing period
- Cefiderocol was well tolerated by neonates and young infants, including pre-term neonates
  - No treatment-related SAEs
  - Only one treatment discontinuation due to non-serious AE
  - Safety profile mirrors morbidity of target population
  - No clinically significant abnormalities (i.e., laboratory test results, vital signs measurements or physical examination findings) were observed in either phase after cefiderocol administration

THANK YOU FOR YOUR ATTENTION

AE, adverse event; CLSI, Clinical and Laboratory Standards Institute; EUCAST, European Committee on Antimicrobial Susceptibility Testing; SAE, serious adverse event.

Back-up slides

Patient Disposition (Safety Population)

Total screened: N=40

- **2 discontinued during screening**
- **8 patient failed inclusion/exclusion criteria**

	Single-dose phase							Multiple-dose phase						
	C1 N=1	C2 N=2	C3 N=3	C4 N=0	C5 N=3	C6 N=3	**Overall N=12**	C1 N=0	C2 N=6	C3 N=1	C4 N=5	C5 N=2	C6 N=4	**Overall N=18**
Patients who received study treatment	1 (100)	2 (100)	3 (100)	0	3 (100)	3 (100)	**12 (100)**	0	6 (100)	1 (100)	5 (100)	2 (100)	4 (100)	**18 (100)**
Completed the study treatment	1 (100)	2 (100)	3 (100)	0	3 (100)	3 (100)	**12 (100)**	0	5 (83.3)	0	3 (60.0)	1 (50.0)	3 (75.0)	**12 (66.7)**
Discontinued the study treatment	0	0	0	0	0	0	0	0	1 (16.7)	1 (100)	2 (40.0)	1 (50.0)	1 (25.0)	6 (33.3)
Reason for treatment discontinuation														
Adverse event	0	0	0	0	0	0	0	0	0	0	0	0	1 (25.0)	1 (5.6)
Recovery[a]	0	0	0	0	0	0	0	0	0	1 (100)	2 (40.0)	0	0	3 (16.7)
Investigator decision	0	0	0	0	0	0	0	0	1 (16.7)	0	0	1 (50.0)	0	2 (11.1)
Study completion status														
Completed the study	1 (100)	2 (100)	3 (100)	0	3 (100)	3 (100)	**12 (100)**	0	6 (100)	1 (100)	5 (100)	2 (100)	4 (100)	**18 (100)**
Did not complete the study	0	0	0	0	0	0	0	0	0	0	0	0	0	0

C1: GA ≥37 weeks and PNA 28 days to <3 months; C2: GA ≥37 weeks and PNA 0 to <28 days; C3: GA ≥32 to 36 weeks and PNA ≥14 days; C4: GA ≥32 to 36 weeks and PNA <14 days; C5: GA ≥26 to <32 weeks and PNA ≥14 days; C6: GA ≥26 to <32 weeks and PNA <14 days.

[a]Recovery from infection and antibiotic treatment is no longer needed.

C, cohort; GA, gestational age; PNA, postnatal age.

Medical History (Safety Population)

	Single-dose phase							Multiple-dose phase						
System Organ Class / Preferred Term	**C1 N=1**	**C2 N=2**	**C3 N=3**	**C4 N=0**	**C5 N=3**	**C6 N=3**	**Overall N=12**	**C1 N=0**	**C2 N=6**	**C3 N=1**	**C4 N=5**	**C5 N=2**	**C6 N=4**	**Overall N=18**
Any, n (%)	**1 (100)**	**2 (100)**	**3 (100)**	**0**	**3 (100)**	**3 (100)**	**12 (100)**	**0**	**6 (100)**	**1 (100)**	**5 (100)**	**2 (100)**	**4 (100)**	**18 (100)**
Blood and lymphatic system disorders	0	0	0	0	2 (66.7)	0	2 (16.7)	0	2 (33.3)	0	1 (20.0)	1 (50.0)	0	4 (22.2)
Congenital, familial and genetic disorders	0	1 (50.0)	1 (33.3)	0	2 (66.7)	0	4 (33.3)	0	4 (66.7)	1 (100)	3 (60.0)	2 (100)	0	**10 (55.6)**
Endocrine disorders	0	0	0	0	0	0	0	0	1 (16.7)	0	0	0	1 (25.0)	2 (11.1)
Eye disorders	0	0	0	0	2 (66.7)	0	2 (16.7)	0	1 (16.7)	0	0	0	0	1 (5.6)
Gastrointestinal disorders	0	0	1 (33.3)	0	2 66.7)	2 (66.7)	5 (41.7)	0	0	0	0	0	0	0
General disorders and administration site conditions	0	0	0	0	0	0	0	0	1 (16.7)	0	1 (20.0)	0	0	2 (11.1)
Infections and infestations	1 (100)	2 (100)	3 (100)	0	3 (100)	1 (33.3)	**10 (83.3)**	0	4 (66.7)	1 (100)	4 (80.0)	2 (100)	3 (75.0)	**14 (77.8)**
Injury, poisoning and procedural complications	0	0	0	0	0	0	0	0	1 (16.7)	0	2 (40.0)	1 (50.0)	1 (25.0)	5 (27.8)
Investigations	0	0	1 (33.3)	0	0	0	1 (8.3)	0	0	1 (100)	0	0	1 (25.0)	2 (11.1)
Metabolism and nutrition disorders	0	1 (50.0)	0	0	1 (33.3)	0	2 (16.7)	0	3 (50.0)	1 (100)	1 (20.0)	0	1 (25.0)	6 (33.3)
Musculoskeletal and connective tissue disorders	0	0	0	0	1 (33.3)	0	1 (8.3)	0	0	0	0	0	0	0
Nervous system disorders	0	1 (50.0)	0	0	0	0	1 (8.3)	0	1 (16.7)	0	0	1 (50.0)	0	2 (11.1)
Pregnancy, puerperium and perinatal conditions	0	1 (50.0)	0	0	3 (100)	3 (100)	**7 (58.3)**	0	1 (16.7)	1 (100)	3 (60.0)	1 (50.0)	3 (75.0)	**9 (50.0)**
Renal and urinary disorders	0	1 (50.0)	0	0	0	0	1 (8.3)	0	0	0	0	0	1 (25.0)	1 (5.6)
Respiratory, thoracic and mediastinal disorders	0	1 (50.0)	2 (66.7)	0	3 (100)	3 (100)	**9 (75.0)**	0	4 (66.7)	1 (100)	4 (80.0)	2 (100)	4 (100)	**15 (83.3)**
Vascular disorders	0	1 (50.0)	0	0	1 (33.3)	0	2 (16.7)	0	0	0	0	0	0	0

C1: GA ≥37 weeks and PNA 28 days to <3 months; C2: GA ≥37 weeks and PNA 0 to <28 days; C3: GA ≥32 to 36 weeks and PNA ≥14 days; C4: GA ≥32 to 36 weeks and PNA <14 days; C5: GA ≥26 to <32 weeks and PNA ≥14 days; C6: GA ≥26 to <32 weeks and PNA <14 days. C, cohort; GA, gestational age; PNA, postnatal age.

Treatment-Emergent Adverse Events – Overall Summary in the Multiple-Dose Phase by Infusion Duration (Safety Population)

	1-hour infusion (N=11)							3-hour infusion (N=7)						
	C1 N=0	C2 N=3	C3 N=1	C4 N=3	C5 N=2	C6 N=2	**Overall N=11**	C1 N=0	C2 N=3	C3 N=0	C4 N=2	C5 N=0	C6 N=2	**Overall N=7**
Any TEAEs, n (%)	0	3 (100)	1 (100)	1 (33.3)	2 (100)	2 (100)	**9 (81.8)**	0	3 (100)	0	2 (100)	0	2 (100)	**7 (100)**
Infections and infestations	0	3 (100)	0	1 (33.3)	2 (100)	2 (100)	**8 (72.7)**	0	2 (66.7)	0	0	0	1 (50.0)	**3 (42.9)**
Metabolism and nutrition disorders	0	2 (66.7)	0	0	2 (100)	2 (100)	**6 (54.5)**	0	0	0	0	0	0	**0**
Blood and lymphatic system disorders	0	0	0	0	2 (100)	2 (100)	**4 (36.4)**	0	0	0	1 (50.0)	0	0	**1 (14.3)**
Respiratory, thoracic and mediastinal disorders	0	1 (33.3)	0	0	1 (50.0)	1 (50.0)	**3 (27.3)**	0	0	0	0	0	1 (50.0)	**1 (14.3)**
Gastrointestinal disorders	0	0	0	0	2 (100)	0	**2 (18.2)**	0	1 (33.3)	0	0	0	0	**1 (14.3)**
Cardiac disorders	0	1 (33.3)	0	0	1 (50.0)	0	**2 (18.2)**	0	0	0	0	0	1 (50.0)	**1 (14.3)**
Investigations	0	1 (33.3)	1 (100)	0	0	1 (50.0)	**3 (27.3)**	0	0	0	0	0	0	**0**
Renal and urinary disorders	0	1 (33.3)	0	0	1 (50.0)	0	**2 (18.2)**	0	0	0	1 (50.0)	0	0	**1 (14.3)**
General disorders and administration site conditions	0	1 (33.3)	0	0	1 (50.0)	0	**2 (18.2)**	0	0	0	0	0	0	**0**

Similar proportion of patients experienced TEAEs after 1-hour or 3-hour infusions

C1: GA ≥37 weeks and PNA 28 days to <3 months; C2: GA ≥37 weeks and PNA 0 to <28 days; C3: GA ≥32 to 36 weeks and PNA ≥14 days; C4: GA ≥32 to 36 weeks and PNA <14 days; C5: GA ≥26 to <32 weeks and PNA ≥14 days; C6: GA ≥26 to <32 weeks and PNA <14 days.
C, cohort; GA, gestational age; PNA, postnatal age; TEAE, treatment-emergent adverse event.

Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Severity (Safety Population)

	Single-dose phase							Multiple-dose phase						
	C1 N=1	C2 N=2	C3 N=3	C4 N=0	C5 N=3	C6 N=3	**Overall N=12**	C1 N=0	C2 N=6	C3 N=1	C4 N=5	C5 N=2	C6 N=4	**Overall N=18**
Any TEAEs, n (%)	1 (100)	1 (50.0)	1 (33.3)	0	2 (66.7)	0	**5 (41.7)**	0	6 (100)	1 (100)	3 (60.0)	2 (100)	4 (100)	**16 (88.9)**
Grade 1 (Mild)	1 (100)	0	0	0	0	0	**1 (8.3)**	0	3 (50.0)	1 (100)	2 (40.0)	0	1 (25.0)	**7 (38.9)**
Grade 2 (Moderate)	0	1 (50.0)	1 (33.3)	0	0	0	**2 (16.7)**	0	2 (33.3)	0	1 (20.0)	1 (50.0)	2 (50.0)	**6 (33.3)**
Grade 3 (Severe)	0	0	0	0	1 (33.3)[a]	0	**1 (8.3)**	0	0	0	0	0	1 (25.0)[e]	**1 (5.6)**
Grade 4 (Life-threatening)	0	0	0	0	0	0	**0**	0	1 (16.7)[c]	0	0	1 (50.0)[d]	0	**2 (11.1)**
Grade 5 (Death)	0	0	0	0	1 (33.3)[b]	0	**1 (8.3)**	0	0	0	0	0	0	**0**
Missing	0	0	0	0	0	0	**0**	0	0	0	0	0	0	**0**

[a]Severe anaemia, large-intestine stenosis, haematological infection, septic shock, hypotension, newborn persistent pulmonary hypertension, stoma prolapse, hyperkalaemia, acute kidney injury, acute respiratory distress syndrome and upper airway obstruction (unrelated) [fatal case].
[b]Life-threatening multiorgan dysfunction syndrome and later sepsis occurred leading to death (unrelated) [fatal case].
[c]Life-threatening neonatal sepsis (unrelated, recovered).
[d]Life-threatening small-intestine perforation, and severe necrotising enterocolitis, thrombocytopenia, suspected fungal sepsis, and hypoalbuminaemia (unrelated).
[e]Severe chronic respiratory disease (unrelated).

C1: GA ≥37 weeks and PNA 28 days to <3 months; C2: GA ≥37 weeks and PNA 0 to <28 days; C3: GA ≥32 to 36 weeks and PNA ≥14 days; C4: GA ≥32 to 36 weeks and PNA <14 days; C5: GA ≥26 to <32 weeks and PNA ≥14 days; C6: GA ≥26 to <32 weeks and PNA <14 days.
C, cohort; GA, gestational age; PNA, postnatal age; TEAE, treatment-emergent adverse event.