Fetroja® – Use in Intraabdominal Infections (IAIs)

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Clinical and PK Studies

- The efficacy and safety of cefiderocol in treating patients with IAIs has not been evaluated in the cefiderocol clinical development program
- PK studies evaluating the intraabdominal penetration of cefiderocol were not conducted during the cefiderocol clinical development program
- **Möhlmann et al (2023)** described a patient case study involving a critically ill patient undergoing CVVH who required cefiderocol treatment via continuous infusion for abdominal sepsis resulting from MDR *Pseudomonas aeruginosa* infection, during which time various PK parameters were evaluated[1]
  - A dose of 4 g of cefiderocol per 24 h provided adequate exposure in order to treat the IAI
  - The estimated unbound plasma concentration of cefiderocol during continuous infusion was 6.8–9.5-fold higher than the target MIC of 2 mg/L for cefiderocol against *P. aeruginosa*

Real-World Evidence

- **PERSEUS** was a retrospective, multicenter, medical chart review study in hospitalized patients (N=261) with Gram-negative bacterial infections throughout Spain[2,3]
  - Adult patients were included if they had a documented Gram-negative bacterial infection (except for *Acinetobacter* spp.) and received cefiderocol continuously for ≥72 h for the first time through the EAP (2018–2022)
    - Patients with *Acinetobacter* spp. infections were enrolled into the ARES study
  - IAIs were identified as the primary infection site in 38 (14.6%) patients, 23 of whom had a confirmed *P. aeruginosa* infection
  - Clinical cure rate in patients with IAIs in the overall population was 68.4% (69.6% for patients with *P. aeruginosa* infection), and 28-day ACM was 23.7% (21.7% for patients with *P. aeruginosa* infection)

- The **PROVE Study** (Retrospective Cefiderocol Chart Review Study) was a retrospective, multicenter, medical chart review study in patients treated with cefiderocol in the US and European hospitals[4–6]
  - The main objectives of PROVE were to describe the patient characteristics and clinical outcomes in patients treated with cefiderocol (for the first time and continuously for ≥72 h) for a documented Gram-negative bacterial infections in real-world settings between November 2020 and February 2024

PROVE Global Final Analysis[4]

- Data are now available from a total of 1075 patients enrolled from US and European medical centers between November 2020 and February 2024
- IAIs were identified as the primary infection site in 67 (6.2%) patients
- Overall, 75.1% of patients had clinical response to cefiderocol treatment at EOT, while 65.7% of patients with IAIs had clinical response at EOT
- Clinical cure was 67.5% in the overall patient population, while 59.7% of patients with IAIs achieved clinical cure

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Real-World Evidence (Cont.)

PROVE US Interim Analysis[5,6]

- 244 patients were enrolled at 15 US medical centers, 12 (4.9%) of which had IAIs as the primary infection site
- Cefiderocol was administered for a median duration of 12 days, 110 patients (45.1%) received cefiderocol for ≥14 days, and 171 patients (70.1%) received concomitant antibiotic treatment
- 5 (41.7%) of the IAI patients achieved clinical cure, 6 (50%) had a clinical response at EOT, while 2 (16.7%) had 14-day in-hospital ACM, and 3 (25%) had 30-day in-hospital ACM (all of whom had monomicrobial IAIs)

Emergency Use Program

- A total of 141 patients were enrolled in a global **Emergency Use Program**, which included cases from the US and various European countries (April 2016 to November 2020). Of the 141 patients, 9% had IAIs mostly due to *P. aeruginosa* (n=7)[7]
  - MICs for cefiderocol in the *P. aeruginosa* isolates originating from an IAI ranged from 0.12–2 µg/mL, with 1 isolate having a MIC >8 µg/mL. A total of 3 out of these 7 patients (43%) achieved clinical response and were alive at Day 28
  - 1 patient with a BSI and cIAI caused by *Acinetobacter baumannii* treated with cefiderocol (MIC=0.25 µg/mL) showed a clinical response and was alive after 28 days of treatment

Retrospective Studies

- **Palermo et al (2023)** retrospectively evaluated 30-day ACM in 41 patients with various infection types, including 8 patients with IAIs, treated with cefiderocol in Italy. In these 8 patients, *A. baumannii* was the most common pathogen (n=6), followed by *Klebsiella pneumoniae* (n=5)[8]
  - The 30-day ACM rate was 62.5% (n=5). Microbiological eradication at EOT was 62.5% (n=5). Clinical cure at EOT and clinical response in first 72 h were 37.5% (n=3) and 75% (n=6), respectively
- **Piccica et al (2023)** retrospectively analyzed 13 patients with IAIs caused by CR Gram-negative bacteria treated with cefiderocol between March 2021 and June 2022 in 3 Italian hospitals. The most common pathogens were *A. baumannii* (63%), *P. aeruginosa* (19%), and *K. pneumoniae* (6%)[9]
  - Of these 13 patients, 4 (31%) patients died within 30 days
  - A multivariate Cox model demonstrated no correlation with IAI and increased risk of 30-day mortality with cefiderocol (HR=1.31; 95% CI, 0.33–5.24; *P*=0.70)
- **Campogiani et al (2023)** conducted a single-center, retrospective, observational study of 11 adult patients treated for CRAB infections with cefiderocol for ≥48 h between May 2021 and September 2022 in Italy[10]
  - Of the 11 patients evaluated, 1 had an IAI. Although early (within 48–72 h of starting cefiderocol) clinical improvement was not achieved, the patient achieved clinical success and survived at 30 days

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Real-World Evidence (Cont.)

Case Reports/Case Series

- **Martinez et al (2022)** presented a case report of a 72-year-old male patient with acute lithiasic pancreatitis who developed abdominal abscess and septic shock caused by pan-resistant *Stenotrophomonas maltophilia*[11]
  - The isolate was sensitive to cefiderocol, and the patient improved clinically and analytically (leukocytes 8.8x10^3/µL, neutrophils 7.13x10^3/µL, and CRP 71.3 mg/L) after receiving compassionate use of cefiderocol 2 g q8h for 21 days
- **Meschiari et al (2021)** described a case series of 4 patients in Italy with IAI caused by XDR/DTR *P. aeruginosa*[12]
  - After receiving cefiderocol combination therapy for 12–23 days, all 4 patients achieved microbiological cure, 3 achieved clinical cure, and 2 survived after EOT
- **Bavaro et al (2021)** described the compassionate use of cefiderocol in combination in 2 patients. 1 patient had septic shock and perihepatic abscess. The second patient developed hepatic abscess and BSI in the setting of hepatic transplantation[13]
  - Both patients recovered and achieved clinical success following cefiderocol combination therapy with no reported AEs
- **Stevens and Clancy (2019)** described a case report of a 46-year-old male patient who had an MDR IAI caused by *P. aeruginosa*[14]
  - Before initiation of treatment, the pathogen was determined to be susceptible to cefiderocol (MIC=0.12 µg/mL)
  - Cefiderocol (750 mg q12h) was successful in completely treating the abscess after 28 days of therapy

Surveillance Studies

- **Bryowsky et al (2023)** evaluated the *in vitro* activity of cefiderocol against CRE and MDR Enterobacterales isolates as part of the SENTRY Antimicrobial Surveillance Program (2020–2022) in US hospitals. The study included 1015 isolates originating from IAIs[15]
  - Cefiderocol susceptibility rates were 83.3% and 95.2% for CRE and MDR Enterobacterales, respectively
- **Nguyen et al (2023)** evaluated the susceptibility of cefiderocol against carbapenem-NS *P. aeruginosa* (n=21), *A. baumannii-calcoaceticus* complex (n=8) and *S. maltophilia* (n=16) overall (no CR *Acinetobacter* from IAIs were included) from IAIs from US hospitals in the SENTRY Antimicrobial Surveillance Program (2020–2022)[16]
  - Cefiderocol susceptibility rates (according to CLSI) for all pathogens were 100%

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Clinical and PK Studies

- The efficacy and safety of cefiderocol in treating IAIs has not been evaluated in the cefiderocol clinical development program
- PK studies evaluating the intraabdominal penetration of cefiderocol were not conducted during the cefiderocol clinical development program

Möhlmann et al (2023) described a patient case study involving a 37-year-old critically ill patient who was readmitted to the ICU for abdominal sepsis caused by MDR *P. aeruginosa* and was treated with cefiderocol via continuous infusion during CVVH.[1]

- After several different antibiotic regimens, treatment was switched to cefiderocol 2 g TID
- 6.5 h after the third dose, cefiderocol was switched to a continuous infusion of 4 g per 24 h, with the daily dose divided into 4 equal 1 g doses infused over 6 h

Results[1]

- On Days 2 and 3 of therapy, total cefiderocol concentrations were measured in intraperitoneal fluid, pre- and postfiltered plasma samples, and ultrafiltrate (urine) samples – see **Table 1**

Table 1. Concentrations of Cefiderocol in Intraabdominal, Arterial, Pre- and Post-Filter and Ultrafiltrate Samples[1]

Sampling Time (h)	Sample Type	Total Concentration (mg/L)
	Arterial	49.8
2 h after ending 3rd prolonged 3-h infusion / 1.5 h before starting continuous infusion[a]		51.6
		62
		56.8
3 h after ending 3rd prolonged 3-h infusion / 0.5 h before starting continuous infusion		15.3
		43
3.5 h after starting continuous infusion		53.9
		52.6
		48.9
		32.6
18.5 h after starting continuous infusion		37.5
		46.3
		45.3
24.5 h after starting continuous infusion[b]	Pre-filter	45.7
	Post-filter	50.5

- After 1 week of therapy, the patient's CRP dropped to 78 mg/L (SOFA score 13) and cefiderocol was stopped due to unavailability; treatment with ceftazidime–avibactam and colistin was resumed
- Throughout continuous infusion, the predicted unbound concentrations of cefiderocol ranged between 13.7 and 19.0 mg/L in arterial samples, while total cefiderocol exposure was up to 915 mg•h/L
- Due to volume extraction during CRRT before fluid substitution, the postfilter concentration of cefiderocol was generally 10–20% above the prefilter concentration
  - In the intraperitoneal drain fluid, the total concentration of cefiderocol was determined to be 15.3 mg/L
- 4 g of cefiderocol per 24 h provided adequate exposure in order to treat the IAI
  - The estimated unbound plasma concentration of cefiderocol during continuous infusion was 6.8–9.5-fold higher than the target MIC of 2 mg/L for cefiderocol against *P. aeruginosa*

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Sampling Time (h)	Sample Type	Total Concentration (mg/L)
2 h after ending 3rd prolonged 3-h infusion / 1.5 h before starting continuous infusion[a]	Arterial	49.8
	Pre-filter	51.6
	Post-filter	62
	Ultrafiltrate	56.8
3 h after ending 3rd prolonged 3-h infusion / 0.5 h before starting continuous infusion	Abdominal drain fluid	15.3
3.5 h after starting continuous infusion	Arterial	43
	Pre-filter	53.9
	Post-filter	52.6
	Ultrafiltrate	48.9
18.5 h after starting continuous infusion	Arterial	32.6
	Pre-filter	37.5
	Post-filter	46.3
24.5 h after starting continuous infusion[b]	Arterial	45.3
	Pre-filter	45.7
	Post-filter	50.5

Arterial: catheter position right jugular vein. The patient's exposure to cefiderocol was estimated with the trapezoidal rule using the concentrations in the arterial samples during continuous infusion and extrapolated to the 24-h area under the concentration–time curve; total clearance was calculated by the infusion rate (mg/h) divided by the arterial plasma concentration.
Abbreviation: h, hour.
[a]Filter age: 15 h.
[b]Filter age: 1 h.
Table adapted from Möhlmann et al. *Br J Clin Pharmacol*. 2023.

– In the intraperitoneal drain fluid, the total concentration of cefiderocol was determined to be 15.3 mg/L

- 4 g of cefiderocol per 24 h provided adequate exposure in order to treat the IAI
  – The estimated unbound plasma concentration of cefiderocol during continuous infusion was 6.8–9.5-fold higher than the target MIC of 2 mg/L for cefiderocol against *P. aeruginosa*

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Retrospective, Medical Chart Review Studies

PERSEUS was a retrospective, multicenter, medical chart review study in hospitalized patients (N=261) with Gram-negative bacterial infections (excluding *Acinetobacter* spp.) throughout Spain.[2]

Methods[2]

Study Design

- Adult patients were included if they had a documented Gram-negative bacterial infection (except for *Acinetobacter* spp.) and received cefiderocol continuously for ≥72 h for the first time through the EAP (2018–2022)
  - Patients with infections caused by *Acinetobacter* spp. were enrolled into the ARES study and were excluded from this study

Outcome Measures

- The main outcomes were clinical cure and ACM at Day 28 in patients treated with cefiderocol for ≥72 h and up to 28 days
  - Clinical cure was defined as the cessation treatment with cefiderocol due to the resolution of symptoms and clinical signs of infection, while clinical success was the composite outcome of clinical cure or survival at Day 28
- The association between the timing of cefiderocol therapy and outcomes was also evaluated

Results[2,3]

- IAIs were identified as the primary infection site in 38 (14.6%) patients in total, 23 of whom had a confirmed *P. aeruginosa* infection
- CCI was highest (4.0) among patients with IAIs, UTIs, and bone/joint infections
- Baseline demographics and clinical characteristics of the 38 patients with IAIs is shown in **Table 2**

Table 2. Baseline Demographics and Clinical Characteristics of Patients with IAIs[3]

IAIs (N=38)	
Age (years), median (IQR)	62 (51–71)
Sex (male), n (%)	31 (81.6)
Admission type, n (%)	
Emergency	23 (60.5)
Scheduled admission	14 (36.8)
Other	1 (2.6)
Any pre-existing medical condition, n (%	33 (86.8)
Diabetes mellitus	5 (13.2)
Solid/hematological tumor	18 (47.4)
Chronic renal disease	6 (15.8)
COPD	3 (7.9)
Chronic liver disease	6 (15.8)
Structural pulmonary disease	0 (0)
Peripheral vascular disease	3 (7.9)
CCI score, median (IQR)	4 (2–5)
SOFA score at baseline, median (IQR)	10 (6–13) N=11
APACHE II score on admission to ICU, median (IQR)	12.5 (8.5–17.5) N=16

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Chronic liver disease	6 (15.8)
Structural pulmonary disease	0 (0)
Peripheral vascular disease	3 (7.9)
CCI score, median (IQR)	4 (2–5)
SOFA score at baseline, median (IQR)	10 (6–13) N'=11
APACHE II score on admission to ICU, median (IQR)	12.5 (8.5–17.5) N'=16

N, overall patient number; N', total number of patients in the category.
Abbreviations: APACHE, acute physiology and chronic health evaluation; CCI, Charlson Comorbidity Index; COPD, chronic obstructive pulmonary disease; IAI, intraabdominal infection; IQR, interquartile range; SOFA, sequential organ failure assessment.
Table adapted from Torre-Cisneros et al. *Eur J Clin Microbiol Infect Dis*. 2025 (Supplementary Material).

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Retrospective, Medical Chart Review Studies

Table 2 (Cont.). Baseline Demographics and Clinical Characteristics of Patients with IAIs[3]

IAIs (N=38)	
ICU, n (%)	17 (44.7)
Mechanical ventilation at baseline, n (%)	12 (31.6)
Septic shock, n (%)	10 (26.3)
Polymicrobial infection, n (%)[a]	8 (21.1)
Baseline Gram-negative species, n (%)	
P. aeruginosa	23 (60.5)
Pseudomonas spp.	3 (7.9)
K. pneumoniae	7 (18.4)
S. maltophilia	2 (5.3)
Meropenem-resistant, n/N' (%)[b]	30/31 (96.8)
Resistant to ceftazidime–avibactam and ceftolozane–tazobactam, n/N' (%)[c]	13/17 (76.5)
Cefiderocol as first-line therapy, n (%)	3 (7.9)
Duration of cefiderocol treatment (days), median (IQR)	10 (7–17)
Combination therapy given with cefiderocol, n (%)[d]	14 (36.8)

N, overall patient number; N', total number of patients in the category.
Abbreviations: IAI, intraabdominal infection; ICU, intensive care unit; IQR, interquartile range.
[a]Primary pathogen in polymicrobial infections, for which cefiderocol was requested, was confirmed by the treating physician.
[b]Susceptibility test results were reported at local site.
[c]Includes patients with susceptibility test results for both ceftazidime–avibactam and ceftolozane–tazobactam.
[d]Includes antibiotics with Gram-negative coverage that have been started before, concomitantly or during the same treatment period.
Table adapted from Torre-Cisneros et al. *Eur J Clin Microbiol Infect Dis*. 2025 (Supplementary Material).

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Retrospective, Medical Chart Review Studies (Cont.)

Results (Cont.)[2,3]

- Clinical cure rate in patients with IAIs in the overall population was 68.4%, and 28-day ACM was 23.7% – see **Figure 1**
- Clinical cure rate in patients with IAIs specifically as a result of *P. aeruginosa* infection was 69.6%, and 28-day ACM was 21.7% – see **Figure 2**
- Clinical cure, 28-Day ACM, and clinical success rates by pathogen in patients with IAIs is shown in **Table 3**

Figure 1. Rates of Clinical Cure at EOT and 28-Day ACM by Infection Site in the Overall Patient Population (N=261)[2]

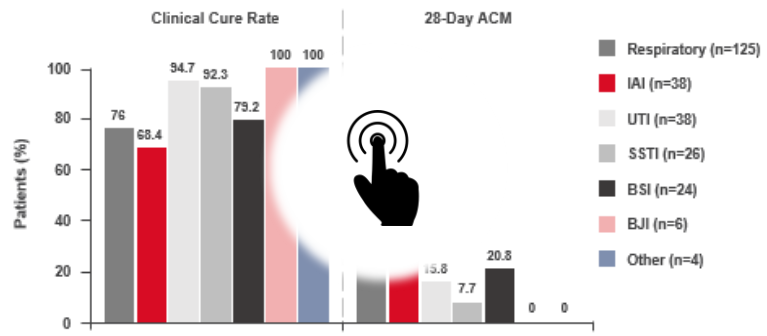


Figure 2. Rates of Clinical Cure at EOT and 28-Day ACM by Infection Site in Patients with *P. aeruginosa* Infections (N=174)[2]

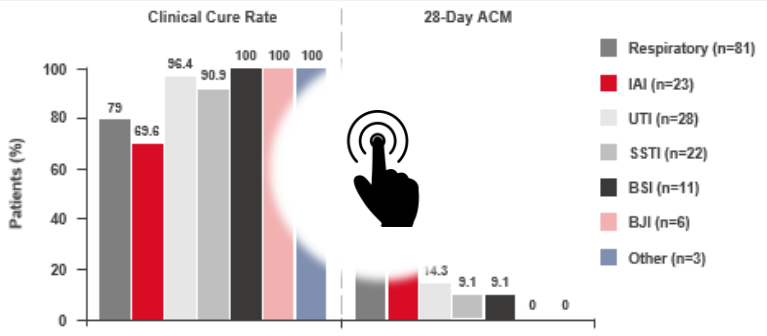


Table 3. Clinical Cure, 28-Day ACM, and Clinical Success Rates by Pathogen in Patients with IAIs[3]

IAIs (N=38)	Clinical Cure at EOT n/N' (%) or n/N' (%)	28-Day ACM by Pathogen n/N (%) or n/N' (%)	Composite Clinical Success n/N (%) or n/N' (%)
Overall	26/38 (68.4)	9/38 (23.7)	29/38 (76.3)
P. aeruginosa	16/23 (69.6)	(21.7)	18/23 (78.3)
Pseudomonas spp.	2/3 (6		3/3 (100)
K. pneumoniae	4/7 (		4/7 (57.1)
Other Enterobacterales	2/2 (		2/2 (100)
S. maltophilia	2/2 (100)	(0)	2/2 (100)
Burkholderia cepacia complex	0/1 (0)	1/1 (100)	0/1 (0)

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Retrospective, Medical Chart Review Studies (Cont.)

Figure 1. Rates of Clinical Cure at EOT and 28-Day ACM by Infection Site in the Overall Patient Population (N=261)[2]

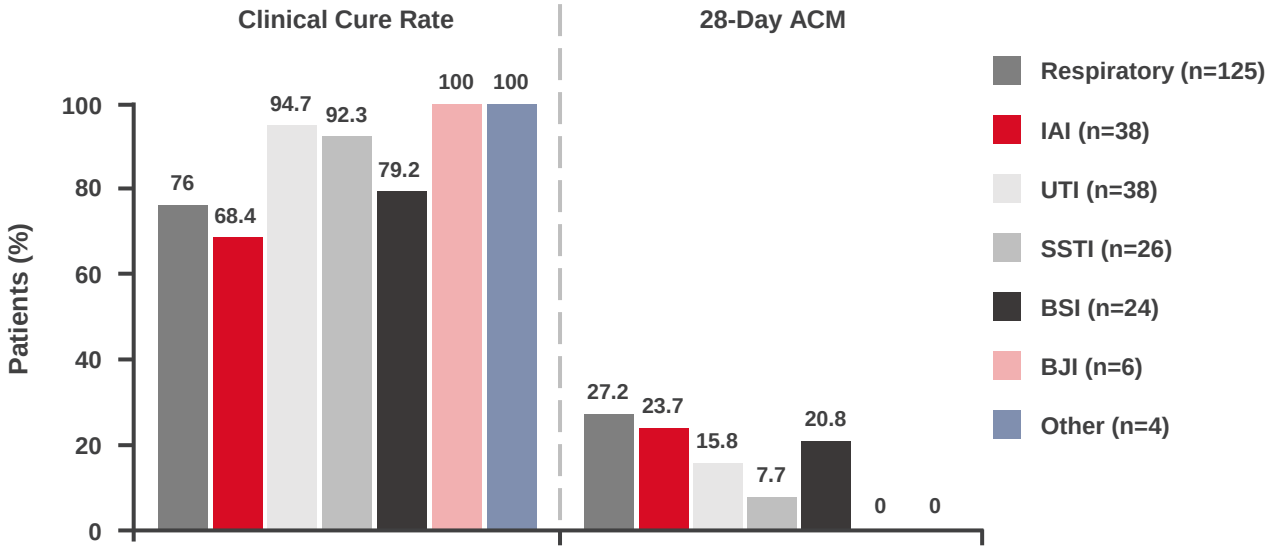
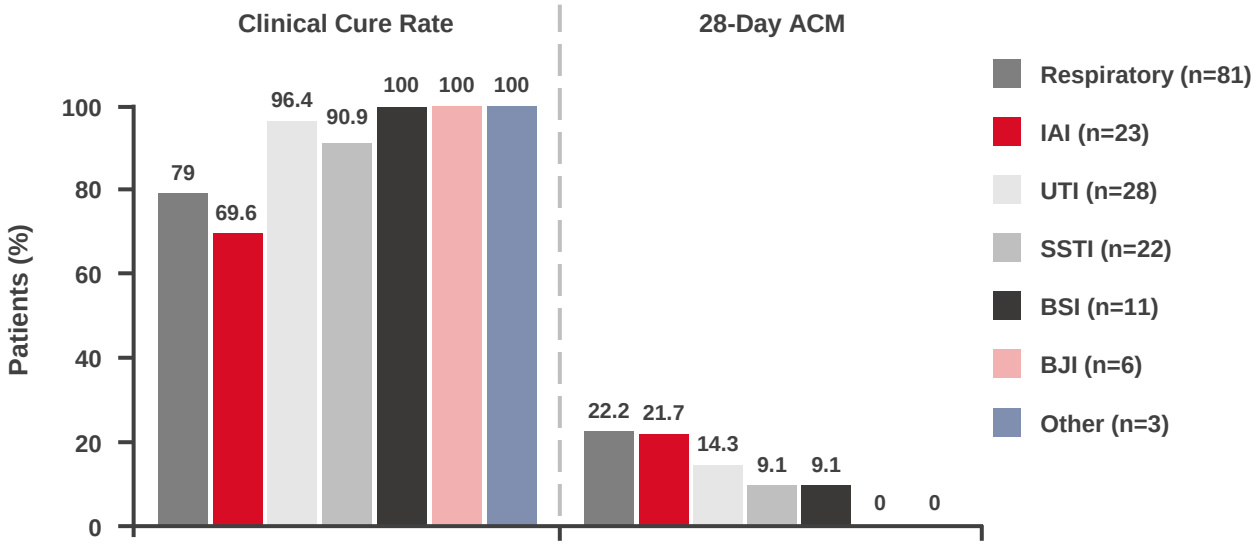


Figure 2. Rates of Clinical Cure at EOT and 28-Day ACM by Infection Site in Patients with *P. aeruginosa* Infections (N=174)[2]



Abbreviations: ACM, all-cause mortality; BJI, bone and joint infection; BSI, bloodstream infection; EOT, end of treatment; IAI, intraabdominal infection; SSTI, skin and soft tissue infection; UTI, urinary tract infection.
Figures adapted from Torre-Cisneros et al. *Eur J Clin Microbiol Infect Dis*. 2025.

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Retrospective, Medical Chart Review Studies (Cont.)

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Overall	26/38 (68.4)	9/38 (23.7)	29/38 (76.3)
P. aeruginosa	16/23 (69.6)	5/23 (21.7)	18/23 (78.3)
Pseudomonas spp.	2/3 (66.7)	0/3 (0)	3/3 (100)
K. pneumoniae	4/7 (57.1)	3/7 (42.9)	4/7 (57.1)
Other Enterobacterales	2/2 (100)	0/2 (0)	2/2 (100)
S. maltophilia	2/2 (100)	0/2 (0)	2/2 (100)
Burkholderia cepacia complex	0/1 (0)	1/1 (100)	0/1 (0)

N, overall patient number; N', total number of patients in the category.
Abbreviations: ACM, all-cause mortality; EOT, end of treatment; IAI, intraabdominal infection.
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Retrospective, Medical Chart Review Studies (Cont.)

The PROVE Study: Background[4–6]

The **PROVE Study** (Retrospective Cefiderocol Chart Review Study) was a multicenter, retrospective, medical chart review study in patients treated with cefiderocol in US and European hospitals. The main objectives of PROVE were to describe the patient characteristics and clinical outcomes in patients treated for the first time with cefiderocol for Gram-negative bacterial infections in real-world settings between November 2020 and February 2024.

- This study included patients with a documented Gram-negative bacterial infection who received cefiderocol for the first time for ≥72 h
  - In addition, patients were included if infection type, cefiderocol start/end dates, daily dose, treatment duration, outcomes at the end of cefiderocol treatment and discharge status (at the end of hospitalization) were known
- Efficacy endpoints included clinical response, clinical cure, ACM at Day 14, ACM at Day 30, and in-hospital mortality
- Documented ADRs that were associated with cefiderocol were evaluated

PROVE: Global Final Analysis[4]

- The US and European medical centers enrolled 1075 patients between November 2020 and February 2024
- The median duration of cefiderocol therapy was 11 days
- Combination therapy was administered to 33.9% of patients
- IAIs were identified as the primary infection site in 67 (6.2%) patients (see **Figure 3**)
- 65.7% of patients with IAIs had clinical response at EOT (see **Figure 4**), while 59.7% of patients with IAIs achieved clinical cure (see **Figure 5**)

Figure 3. Distribution of Primary Infection Sites[4]

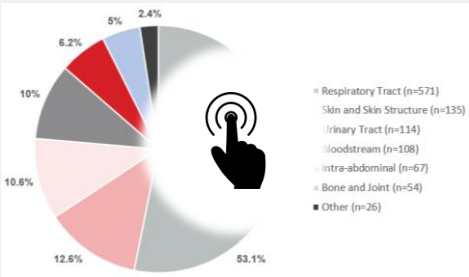


Figure 4. Rates of Clinical Response at EOT by Infection Site in the Overall Patient Population[4]

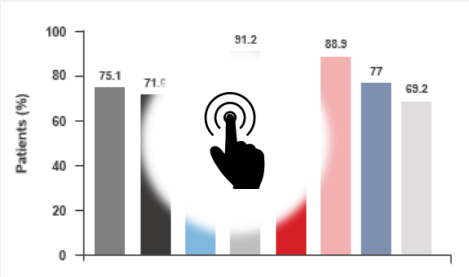
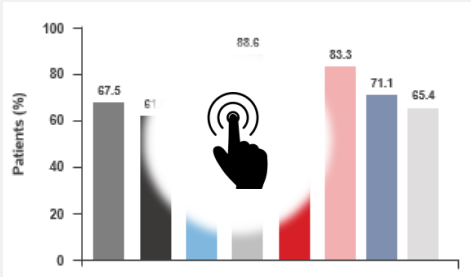


Figure 5. Rates of Clinical Cure at EOT by Infection Site in the Overall Patient Population[4]

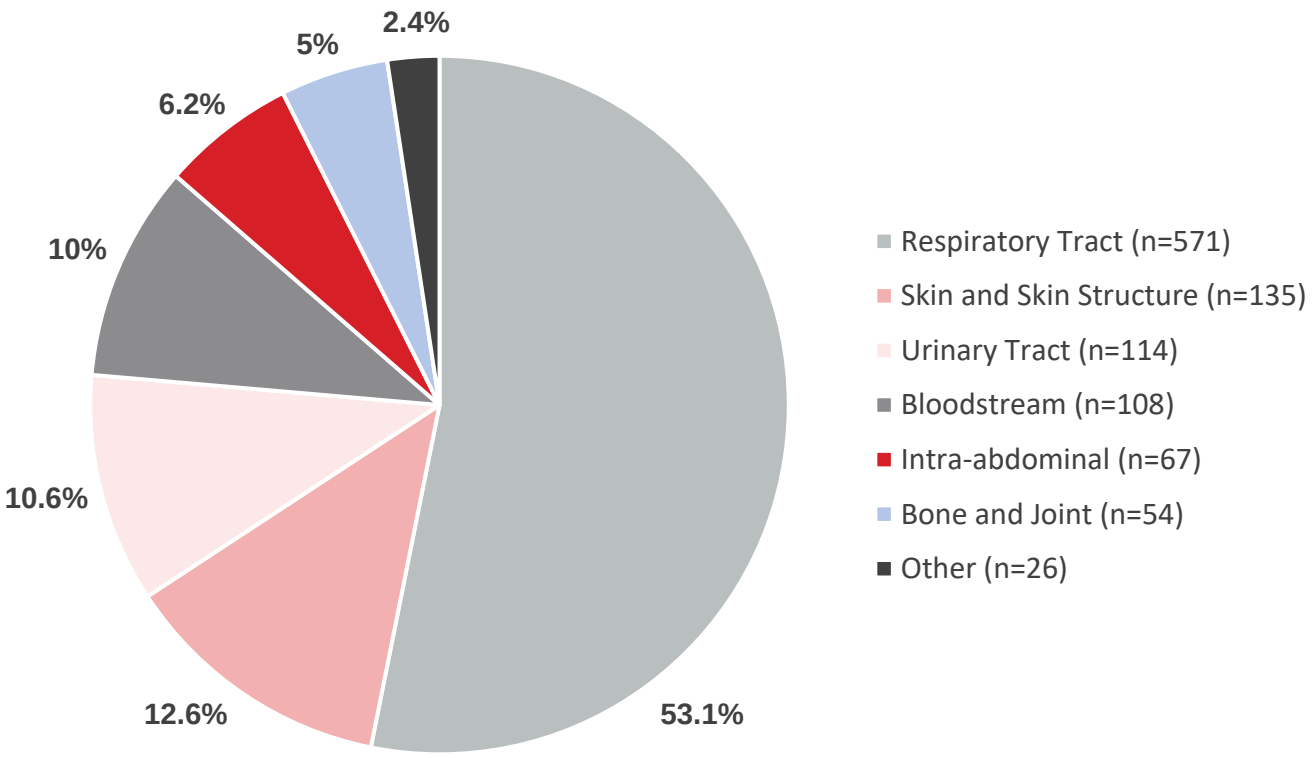


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Retrospective, Medical Chart Review Studies (Cont.)

Figure 3. Distribution of Primary Infection Sites[4]



Other: bone and joint, skin and skin structure, intraabdominal, and other sites.
Figure adapted from Clancy et al. IDWeek. 2024.

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Retrospective, Medical Chart Review Studies (Cont.)

Figure 4. Rates of Clinical Response at EOT by Infection Site in the Overall Patient Population[4]

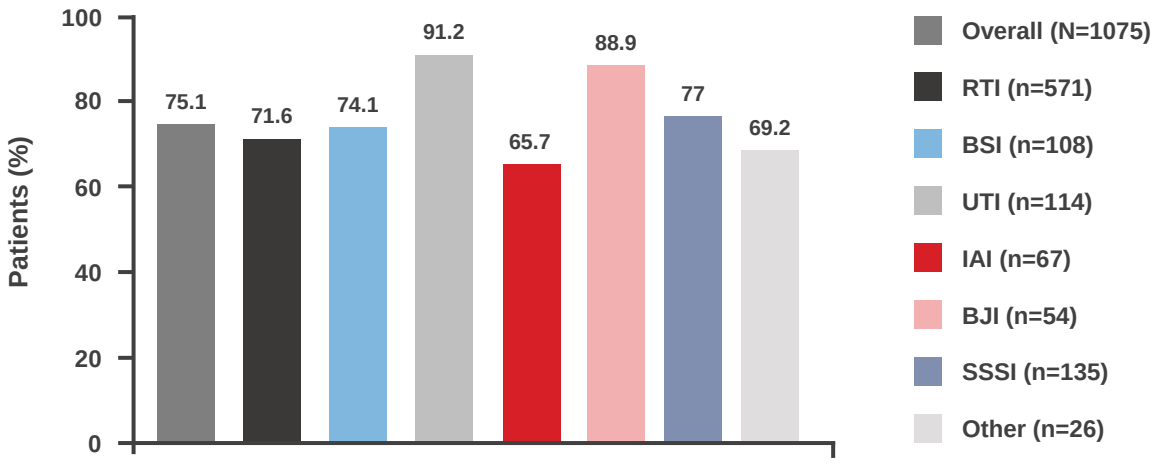
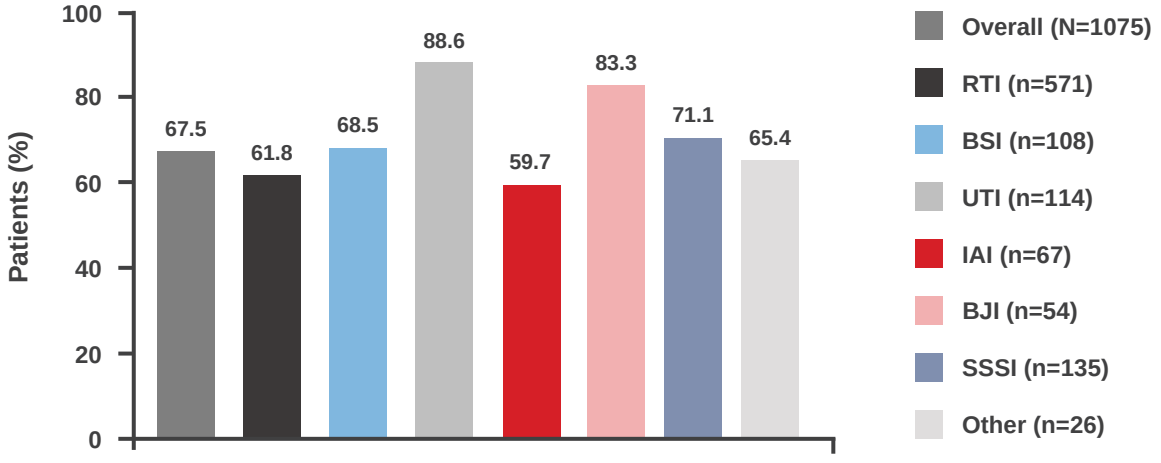


Figure 5. Rates of Clinical Cure at EOT by Infection Site in the Overall Patient Population[4]



Abbreviations: BJI, bone and joint infection; BSI, bloodstream infection; EOT, end of treatment; IAI, intraabdominal infection; SSSI, skin and skin structure infection; RTI, respiratory tract infection; UTI, urinary tract infection.
Figures adapted from Clancy et al. IDWeek. 2024.

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Retrospective, Medical Chart Review Studies (Cont.)

PROVE: US Interim Analysis[5,6]

- 244 patients were enrolled at 15 US medical centers between November 2020 and March 2023
- The median (IQR) age of patients was 56 (43.5–65) years, 61.5% of patients were male, while 66.4% of patients were admitted from an urgent or emergency unit
- Cefiderocol was administered for a median duration of 12 days, 110 patients (45.1%) received cefiderocol for ≥14 days, and 171 patients (70.1%) received concomitant antibiotic treatment
- IAIs were identified in 12 (4.9%) patients as the primary infection site – see **Figure 6**
- Severity of illness and use of cefiderocol in this sub-population of patients is shown in **Table 4**
- 7 (58.3%) of the 12 patients with IAIs had a monomicrobial infection, of which 2 (28.6%) achieved clinical cure, 3 (42.9%) had a clinical response at EOT, while 2 (28.6%) had 14-day in-hospital ACM, and 3 (42.9%) had 30-day in-hospital ACM – see **Table 5**
- 5 (41.7%) of the 12 patients with IAIs had a polymicrobial infection, of which 3 (60%) achieved clinical cure, 3 (60%) had a clinical response at EOT, while none (0%) had either 14-day or 30-day in-hospital ACM – see **Table 5**
- 1 patient with an IAI had a relapse/reinfection after the end of cefiderocol treatment

Figure 6. Primary Infection Sites (Overall; N=244)[5]

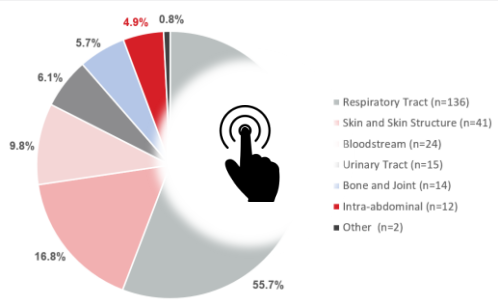


Table 4. Severity of Illness and Cefiderocol Use in Patients with IAIs[6]

IAIs (N=12)	
Age ≥65 years, n (%)	3 (25)
Male, n (%)	9 (75)
ICU stay when cefiderocol was initiated or within 2 days after initiation of cefiderocol, n (%)[a]	7 (58.3)
Received organ support when cefiderocol was initiated or within 2 days after initiation of cefiderocol, n (%)	6 (50)
Polymicrobial infections by pathogen	3/5 (60)
Organ support type, n (%)[b]	
Mechanical ventilation	5 (41.7)
CRRT	1 (8.3)
ECMO	1 (8.3)
Vasopressor use	4 (33.3)
Dialysis[c]	0 (0)
Antimicrobials or antifungals used p	5 (41.7)
Reason for starting cefiderocol, n (%)	
Documented infection	6 (50)
Empiric for suspected CR Gram-negative ba	2 (16.7)
Salvage treatment	2 (16.7)
Other including unknown	2 (16.7)
Time from admission to sampling of a positive culture resulting in cefiderocol use, days, median (Q1–Q3)[d]	19 (6.5–37.5)
Time from sampling of a positive culture to first cefiderocol dose, days, median (Q1–Q3)	5.5 (2.5–6)
Duration of cefiderocol treatment, days, median (Q1–Q3)	11 (6.5–33.5)

Table 5. Distribution of Pathogens, Clinical Cure, Clinical Response at EOT, and 30-Day In-Hospital ACM in Patients with IAIs[6]

IAIs (N=12)	Pathogen n (%)	Clinical Cure n/N[a] (%)	Clinical Response at EOT, n/N[a] (%)	30-Day In-Hospital ACM, n/N[a] (%)
Monomicrobial infections by pathogen	7 (58.3)	2/7 (28.6)	3/7 (42.9)	3/7 (42.9)
P. aeruginosa	2 (16.7)	1/2 (50)	1/2 (50)	1/2 (50)
Enterobacterales			1/4 (25)	2/4 (50)
S. maltophilia			1/1 (100)	0/1 (0)
Polymicrobial infections by pathogen			3/5 (60)	0/5 (0)
A. baumannii + other Gram-negative species			0/1 (0)	0/1 (0)
A. baumannii + *P. aeruginosa*			0/1 (0)	0/1 (0)
P. aeruginosa + other Gram-negative species	3 (25)	2/3 (66.7)	2/3 (66.7)	0/3 (0)
P. aeruginosa + Enterobacterales	3 (25)	2/3 (66.7)	2/3 (66.7)	0/3 (0)
Any other combination of 2 pathogens	1 (8.3)	1/1 (100)	1/1 (100)	0/1 (0)

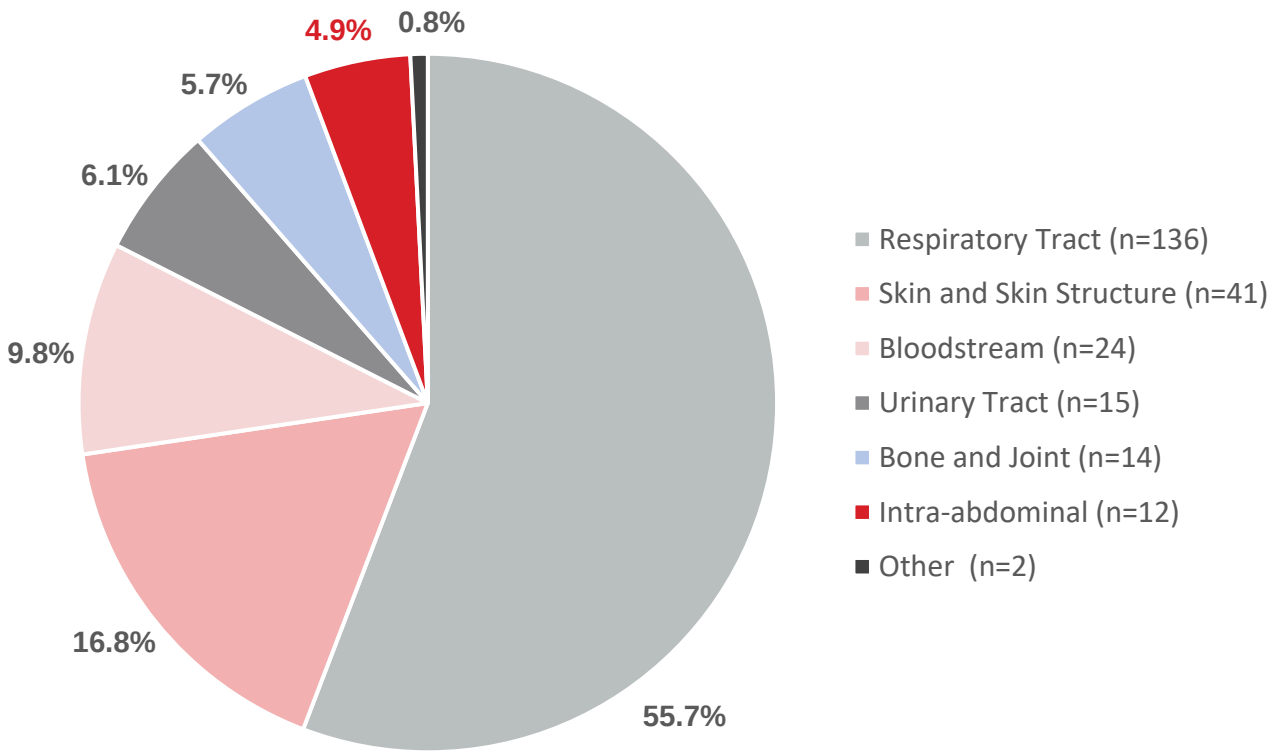
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Retrospective, Medical Chart Review Studies (Cont.)

Figure 6. Primary Infection Sites (Overall; N=244)[5]



Other: Single site not in any of the above categories.
Figure adapted from Clancy et al. *Infect Drug Resist*. 2024.

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Mechanical ventilation	5 (41.7)
CRRT	1 (8.3)
ECMO	1 (8.3)
Vasopressor use	4 (33.3)
Dialysis[c]	0 (0)
Antimicrobials or antifungals used prior to cefiderocol, n (%)	5 (41.7)
Reason for starting cefiderocol, n (%)	
Documented infection	6 (50)
Empiric for suspected CR Gram-negative bacterial infection	2 (16.7)
Salvage treatment	2 (16.7)
Other including unknown	2 (16.7)
Time from admission to sampling of a positive culture resulting in cefiderocol use, days, median (Q1–Q3)[d]	19 (6.5–37.5)
Time from sampling of a positive culture to first cefiderocol dose, days, median (Q1–Q3)	5.5 (2.5–6)
Duration of cefiderocol treatment, days, median (Q1–Q3)	11 (6.5–33.5)

Data are expressed as a percentage of the total number of patients within the subgroup (n/N).
Abbreviations: CR, carbapenem-resistant; CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation; IAI, intraabdominal; ICU, intensive care unit; Q, quartile.
[a]ICU stay only includes patients with ICU stay during which cefiderocol was initiated or for which stay admission occurred within 2 days of initiating cefiderocol.
[b]Types of organ support are not mutually exclusive.
[c]Cefiderocol was initiated for 1 patient while receiving dialysis and was admitted to the ICU 7 days later (while receiving both cefiderocol and dialysis).
[d]Index culture sample closest to initiation of cefiderocol treatment may have been collected and tested in outpatient settings prior to hospitalization.
Table adapted from Clancy et al. *Infect Drug Resist*. 2024 (Supplementary Material).

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Retrospective, Medical Chart Review Studies (Cont.)

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IAIs (N=12)	Pathogen n (%)	Clinical Cure n/N' (%)	Clinical Response at EOT, n/N' (%)	30-Day In-Hospital ACM, n/N' (%)
Monomicrobial infections by pathogen	7 (58.3)	2/7 (28.6)	3/7 (42.9)	3/7 (42.9)
P. aeruginosa	2 (16.7)	1/2 (50)	1/2 (50)	1/2 (50)
Enterobacterales	4 (33.3)	1/4 (25)	1/4 (25)	2/4 (50)
S. maltophilia	1 (8.3)	0/1 (0)	1/1 (100)	0/1 (0)
Polymicrobial infections by pathogen	5 (41.7)	3/5 (60)	3/5 (60)	0/5 (0)
A. baumannii + other Gram-negative species	1 (8.3)	0/1 (0)	0/1 (0)	0/1 (0)
A. baumannii + *P. aeruginosa*	1 (8.3)	0/1 (0)	0/1 (0)	0/1 (0)
P. aeruginosa + other Gram-negative species	3 (25)	2/3 (66.7)	2/3 (66.7)	0/3 (0)
P. aeruginosa + Enterobacterales	3 (25)	2/3 (66.7)	2/3 (66.7)	0/3 (0)
Any other combination of 2 pathogens	1 (8.3)	1/1 (100)	1/1 (100)	0/1 (0)

Data are expressed as a percentage of the total number of patients within a subgroup (n/N or n/N').
Abbreviations: ACM, all-cause mortality; EOT, end of treatment; IAI, intraabdominal infection.
Table adapted from Clancy et al. *Infect Drug Resist*. 2024 (Supplementary Material).

- 1 patient with an IAI had a relapse/reinfection after the end of cefiderocol treatment

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Emergency Use Program

Longshaw et al (2021) described clinical outcomes and the susceptibility of isolates from patients treated with cefiderocol who were enrolled in a global Emergency Use Program (April 2016 to November 2020), before cefiderocol regulatory authorization and market access was available in Europe. Compassionate use was granted for patients with infections caused by Gram-negative pathogens who had no alternative treatment options (pathogens were resistant to alternative antibiotics or had a documented unacceptable toxicity).[7]

Methods[7]

- Patients (N=141) originating from 12 countries with various infection sites including IAIs, received cefiderocol treatment. A diverse patient population with several comorbidities (eg, burns, organ transplant, COVID-19) was evaluated with ages ranging from 5 months to 84 years
- Multiple pathogens were identified, with the most common being *P. aeruginosa* (50%)
- Susceptibility was determined by broth microdilution or disc diffusion and was interpreted using EUCAST breakpoints (non-species related PK/PD breakpoints were used when no clinical breakpoints were available)

Results[7]

- A total of 9% of patients who received cefiderocol treatment had an IAI. Clinical outcomes (clinical response and resolution) were determined by the patients' treating physician and were reported for a total of 102 patients (118 isolates) with available cefiderocol susceptibility data
- **Table 6** shows the clinical outcomes for IAIs caused by *P. aeruginosa* (n=7), of which, 3 (43%) showed a clinical response and were alive after 28 days of cefiderocol treatment

Table 6. Clinical Outcomes by Cefiderocol Susceptibility in Infections caused by *P. aeruginosa*[7]

Infection Site	MIC (µg/mL)	Disc ZD	CRM[a]	Clinical Response	28-Day Mortality
cIAI/abscess	0.12	22		Responded	Survived
IAI	0.25			No Response	Death
cIAI/sepsis	1			Responded	Survived
cIAI/pleural empyema/ decubitus ulcer/BSI	2			No Response	Death
cIAI	2			No Response	Death
cIAI (wound infection)[b]		19		Responded	Survived
RTI + IAI[b]	>8	26	VIM-2	No Response	Death

- 1 patient with a BSI/cIAI caused by *A. baumannii* treated with cefiderocol (MIC=0.25 µg/mL) showed a clinical response and was alive after 28 days of treatment

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cIAI/pleural empyema/ decubitus ulcer/BSI	2			No Response	Death
cIAI	2			No Response	Death
cIAI (wound infection)[b]		19		Responded	Survived
RTI + IAI[b]	>8	26	VIM-2	No Response	Death

Abbreviations: BSI, bloodstream infection; cIAI, complicated intraabdominal infection; CRM, carbapenem resistance mechanism; IAI, intraabdominal infection; MIC, minimum inhibitory concentration; RTI, respiratory tract infection; VIM, Verona integron-encoded metallo-β-lactamase; ZD, zone diameter.
[a]CRM defined as carbapenem resistance mechanism (when available).
[b]Cefiderocol-resistant isolate based on MIC >2 µg/mL or ZD <22 mm in the absence of MIC value.
Table adapted from Longshaw et al. ECCMID. 2021.

- 1 patient with a BSI/cIAI caused by *A. baumannii* treated with cefiderocol (MIC=0.25 µg/mL) showed a clinical response and was alive after 28 days of treatment

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Retrospective Studies

Palermo et al (2023) conducted a retrospective study which included 8 patients with IAIs treated with cefiderocol between September 2021 and July 2022 in Palermo, Italy. Cefiderocol 2 g q8h over 3 h (with adjustments for renal impairment) was administered.[8]

- The primary outcome was 30-day ACM. Secondary outcomes included clinical cure at EOT, clinical response in the first 72 h of treatment, and microbiological eradication
- Of the 8 patients with IAIs, 3 (37.5%) had a polymicrobial infection. 6 (75%) *A. baumannii* isolates and 5 *K. pneumoniae* isolates were identified. Outcome details are provided in **Table 7**

Table 7. 30-Day ACM and Secondary Outcomes in Patients with IAIs Treated with Cefiderocol (n=8)[8]

Monotherapy n (%)	Combination Therapy n (%)	30-Day ACM n (%)	Microbiological Eradication at EOT[a] n (%)	Clinical Cure at EOT[b] n (%)	Clinical Response in First 72 h[c] n (%)	Days of Therapy Median (IQR)
4 (50%)	4 (50%)	5 (62.5%)	5 (62.5%)	3 (37.5%)	6 (75%)	10 (4–24)

Abbreviations: ACM, all-cause mortality; EOT, end of therapy; h, hours; IQR, interquartile range.
[a]Defined as documented or presumed eradication of isolated bacteria at EOT.
[b]Defined as symptom resolution and clearance of inflammatory markers.
[c]Defined as an initial clinical response in which it was not necessary to switch therapy, or the patient did not die.
Table adapted from Palermo et al. *Antibiotics (Basel)*. 2023.

Piccica et al (2023) performed a retrospective analysis of patients with CR Gram-negative bacterial infections occurring in 3 Italian hospitals from March 2021 to June 2022. Of 142 total patients included, 13 had an IAI.[9]

Methods[9]

- The analysis included adult patients (ages ≥18 years) with microbiologically documented MDR and DTR Gram-negative infections (eg, CRE, CRAB, and DTR *P. aeruginosa*), who received treatment with cefiderocol, for ≥3 days
- Patients were given cefiderocol 2 g q8h which was adjusted based on renal function
- The most common pathogen was *A. baumannii* (63%)
- The primary outcome was 30-day mortality. Additionally, a multivariate Cox model was performed to assess for predictors of 30-day mortality

Results[9]

- A total of 13 patients had an IAI. Of these 13 patients, 7 (10%) were treated with cefiderocol monotherapy and 6 (8.3%) were treated with combination therapy
- Of the 13 patients with IAIs, 4 (31%) died at 30 days
- The multivariate Cox model showed no association with IAI and 30-day mortality (HR=1.31; 95% CI, 0.33–5.24; *P*=0.70)

Retrospective Studies (Cont.)

Campogiani et al (2023) conducted a single-center, retrospective, observational study of 11 adult patients who received cefiderocol for CRAB infections for ≥48 h between May 2021 and September 2022 in Rome, Italy.[10]

- Of the 11 patients enrolled, 1 patient had an IAI and was treated with cefiderocol 2 g q8h as monotherapy for 10 days
- Outcome details are provided in **Table 8**

Table 8. Early Clinical Improvement and Secondary Outcomes in a Patient with an IAI Treated with Cefiderocol[10]

Age/Sex	Early Clinical Improvement[a]	Clinical Success[b]	30-Day Death
70/F	No	Yes	Survived

Abbreviations: CRP, C-reactive protein; h, hours; IAI, intraabdominal infection; PCT, procalcitonin.
[a]Early clinical improvement was defined as ≥1 of the following within 48–72 h from initiating cefiderocol: resolution of signs/symptoms of infection, no fever for ≥48 consecutive h, interruption of inotropic agents if needed at initiation of antibiotic, reduction of CRP concentration of ≥75% of the maximum concentration, or reduction of PCT concentration of ≥80% of the maximum concentration or PCT <0.5 ng/mL.
[b]Clinical success is defined as the composite endpoint of absence of signs and symptoms of *A. baumannii* infection and 14-day survival after discontinuing cefiderocol.
Table adapted from Campogiani et al. *Open Forum Infect Dis*. 2023.

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Case Reports/Case Series

Martinez et al (2022) presented a case report on the compassionate use of cefiderocol in a 72-year-old male with acute lithiasic pancreatitis, cholecystectomy, and chronic liver disease. He received piperacillin–tazobactam, linezolid, and meropenem during his hospital admission.[11]

- On Day 30, the patient experienced an episode of septic shock secondary to a retroperitoneal collection found in the pararenal space. *S. maltophilia* (sensitive to levofloxacin and resistant to cotrimoxazole [antibiotic of choice]) was isolated from a culture of the drained fluid
- On Day 60, the patient had a subsequent episode of septic shock and a culture of *S. maltophilia* was pan-resistant to all commercially available antibiotics, but sensitive to cefiderocol. He received compassionate use of cefiderocol 2g q8h as monotherapy for 21 days
- The patient became afebrile after 7 days of therapy and improved clinically and analytically (leukocytes 8.8x10^3/µL, neutrophils 7.13x10^3/µL, and CRP 71.3 mg/L)
- No AEs related to cefiderocol were reported

Meschiari et al (2021) described case reports of 17 patients in Italy with XDR/DTR *P. aeruginosa* infections who failed treatment on other regimens before initiating therapy with cefiderocol. There were 4 cases of cIAI. 2 patients had peritonitis with retroperitoneal abscesses, 1 patient developed cholangitis with underlying cholangiocarcinoma, and 1 patient had aortic graft infection and peritonitis – see **Table 9**.[12]

- Of the 4 patients, all achieved microbiological cure, 3 patients demonstrated clinical cure, and 2 survived. 1 patient who demonstrated clinical failure did not survive. The patient who demonstrated both clinical and microbiological cure died 23 days after EOT
- No AEs were reported and there was no relapse or recurrence of infection in these patients

Table 9. Description of Patient Characteristics and Outcomes in Patients with IAI[12]

Age/ Sex	Underlying Conditions	Isolated Pathogen and Cefiderocol MIC (µg/mL)	Type of Infection	Initial Treatment Regimen	Cefiderocol Dose and Days of Therapy (days)	Combination with Cefiderocol	Outcome (After 7 Days from EOT)	Death (Days After EOT)
64/F	Recurrent cholangitis; carcinoma	XDR/DTR-P 0.5	Cholangitis	CZA + AMK	2 g q8h (CRRT), 1g q8h (12)	FOF	CF, MC	Yes (3)[a]
74/M	Rupture abdominal aortic aneurysm; colon perforation	XDR/DTR-P NA	Aortic g infecti perito		(15)	CZA	CC, MC	No
50/F	Acute necrotic-hemorrhagic pancreatitis	XDR/DTR-P ≤2	Peritoniti retroperito abscess		h (21)	CIP	CC, MC	Yes (23)[a]
58/M	Pancreatic cancer, pancreatectomy	XDR/DTR-P ≤2	Peritonitis and retroperitoneal abscess; BSI	CZA + TGC	1.5 g q8h (CRRT) (10), 2 g q8h (13)	TGC + RIF	CC, MC	No

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64/F	Recurrent cholangitis; carcinoma	XDR/DTR-P 0.5	Cholangitis	CZA + AMK + ATM	2 g q8h (CRRT), 1g q8h (12)	FOF	CF, MC	Yes (3)[a]
74/M	Rupture abdominal aortic aneurysm; colon perforation	XDR/DTR-P NA	Aortic graft infection; peritonitis	CZA + FOS + AMK	1.5 g q8h (15)	CZA	CC, MC	No
50/F	Acute necrotic-hemorrhagic pancreatitis	XDR/DTR-P ≤2	Peritonitis and retroperitoneal abscess	C/T + CIP + AMK	2 g q8h (21)	CIP	CC, MC	Yes (23)[a]
58/M	Pancreatic cancer, pancreatectomy	XDR/DTR-P ≤2	Peritonitis and retroperitoneal abscess; BSI	CZA + TGC	1.5 g q8h (CRRT) (10), 2 g q8h (13)	TGC + RIF	CC, MC	No

Abbreviations: AMK, amikacin; ATM, aztreonam; BSI, bloodstream infection; CC, clinical cure, CF, clinical failure; CIP, ciprofloxacin; CRRT, continuous renal replacement therapy; C/T, ceftolozane–tazobactam; CZA, ceftazidime–avibactam; DTR-P, difficult-to-treat *P. aeruginosa*; EOT, end of treatment; F, female; FOS, fosfomycin IV; M, male; MC, microbiological cure; MIC, minimum inhibitory concentration; NA, not available; q8h, every 8 hours; RIF, rifampicin; TGC, tigecycline; XDR, extensively drug-resistant.

[a]( ) number of days after EOT that death occurred.

Table adapted from Meschiari et al. *JAC Antimicrob Resist*. 2021.

Fetroja® – Use in Intraabdominal Infections (IAIs)

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Case Reports/Case Series (Cont.)

Bavaro et al (2021) reported on combination therapy with cefiderocol in 13 compassionate use cases treated between September 1, 2020 through March 31, 2021.[13]

- Of the 13 patients, 2 (15%) had cIAI, 1 patient presented to the ICU with septic shock and perihepatic abscess. The second patient developed sepsis secondary to hepatic abscess and BSI in the setting of hepatic transplantation
- Both patients failed initial antibiotic combination therapy with unsatisfactory clinical responses and were started on a subsequent cefiderocol (2 g q8h)-based treatment for a median of 24 days (range 21–28 days)
- Both patients recovered and achieved clinical success with no reported AEs
- **Table 10** shows the characteristics and clinical outcomes for these patients

Table 10. Characteristics and Outcomes in Patients with IAIs[13]

Age/ Sex	Cause of Hospitalization	Underlying Disease	Pathogen	Type of Infection	Initial Therapy (Days)	Cause of Failure	Cefiderocol-Based Therapy (Days)	Outcome	Outcome at 30 Days
25/M	Subocclusion and volvulus treated with gut surgical resection	Colostomy, hip and arm fracture	Poly-microbial[a]	P...	...	...satisfactory ...linical ...sponse	Cefiderocol, TGC, DAP, FOS (21)	Recovery	Success
60/M	Sepsis	Hepatic transplantation for HBV-related cirrhosis and HCC, previous ischemic heart disease	CR-Kp (KPC)	a... B...	...	...satisfactory clinical response	Cefiderocol, TGC, CST (17), then cefiderocol, FOS (11)[b]	Recovery	Success

Stevens and Clancy (2020) described a case report detailing compassionate use of cefiderocol to treat a 46-year-old male for an IAI caused by MDR *P. aeruginosa*.[14]

- Treatment with polymyxins and aminoglycosides was avoided due to life-threatening toxicities
- Sensitivity to cefiderocol was determined based on an MIC of 0.12 µg/mL obtained from the abdomen before initiation of treatment and from the abdominal drain on Day 2 of cefiderocol therapy
- Cefiderocol was successful in completely treating the abscess after 28 days of therapy – see **Table 11**

Table 11. Compassionate Use of Cefiderocol to Treat a Patient with an IAI due to MDR *P. aeruginosa*[14]

Infection Type	Causative Pathogen	Concomitant Antibiotics	C...	Cefiderocol Treatment Duration, Days	Reported SAEs	Patient Outcome
Intraabdominal abscess	MDR *P. aeruginosa*	Metronidazole 500 mg q8h		28	None	Clinical success

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Case Reports/Case Series (Cont.)

Table 10. Characteristics and Outcomes in Patients with IAIs[13]

Age/ Sex	Cause of Hospitalization	Underlying Disease	Pathogen	Type of Infection	Initial Therapy (Days)	Cause of Failure	Cefiderocol-Based Therapy (Days)	Outcome	Outcome at 30 Days
25/M	Subocclusion and volvulus treated with gut surgical resection	Colostomy, hip and arm fracture	Poly-microbial[a]	Perihepatic abscess, Septic shock	MEM, TGC, DAP, FOS (5)	Unsatisfactory clinical response	Cefiderocol, TGC, DAP, FOS (21)	Recovery	Success
60/M	Sepsis	Hepatic transplantation for HBV-related cirrhosis and HCC, previous ischemic heart disease	CR-Kp (KPC)	Hepatic abscess, BSI	TGC, CZA, CST (3)	Unsatisfactory clinical response	Cefiderocol, TGC, CST (17), then cefiderocol, FOS (11)[b]	Recovery	Success

Abbreviations: BSI, bloodstream infection; CRAB, carbapenem-resistant *A. baumannii*; CR-Kp, carbapenem-resistant *K. pneumoniae*; CST, colistin; CZA, ceftazidime–avibactam; DAP, daptomycin; FOS, fosfomycin IV; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; M, male; MEM, meropenem; MDR, multidrug-resistant; TGC, tigecycline.
[a]CRAB, MDR-*Enterobacter cloacae* complex, *Morganella morganii*, ampicillin-resistant *Enterococcus faecium*.
[b]Changed for toxicity (decreased renal function, bilirubin increased).
Table adapted from Bavaro et al. *Antibiotics (Basel)*. 2021.

- Treatment with polymyxins and aminoglycosides was avoided due to life-threatening toxicities
- Sensitivity to cefiderocol was determined based on an MIC of 0.12 µg/mL obtained from the abdomen before initiation of treatment and from the abdominal drain on Day 2 of cefiderocol therapy
- Cefiderocol was successful in completely treating the abscess after 28 days of therapy (**Table 11**)

Table 11. Compassionate Use of Cefiderocol to Treat a Patient with an IAI due to MDR *P. aeruginosa*[14]

Infection Type	Causative Pathogen	Concomitant Antibiotics	Cefiderocol Treatment Duration, Days	Reported SAEs	Patient Outcome
Intraabdominal abscess	MDR *P. aeruginosa*	Metronidazole 500 mg q8h	28	None	Clinical success

Fetroja® – Use in Intraabdominal Infections (IAIs)

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Case Reports/Case Series (Cont.)

Table 11. Compassionate Use of Cefiderocol to Treat a Patient with an IAI due to MDR *P. aeruginosa*[14]

Infection Type	Causative Pathogen	Concomitant Antibiotics	Cefiderocol Dose and Regimen	Cefiderocol Treatment Duration, Days	Reported SAEs	Patient Outcome
Intraabdominal abscess	MDR *P. aeruginosa*	Metronidazole 500 mg q8h	750 mg q12h	28	None	Clinical success

Abbreviations: MDR, multidrug-resistant; q8h, every 8 hours; q12h, every 12 hours; SAE, serious adverse event.
Table adapted from Stevens et al. *Pharmacotherapy*. 2019.

Stevens and Clancy (2020) described a case report detailing compassionate use of cefiderocol to treat a 46-year-old male for an IAI caused by MDR *P. aeruginosa*.[14]

- Treatment with polymyxins and aminoglycosides was avoided due to life-threatening toxicities
- Sensitivity to cefiderocol was determined based on an MIC of 0.12 µg/mL obtained from the abdomen before initiation of treatment and from the abdominal drain on Day 2 of cefiderocol therapy
- Cefiderocol was successful in completely treating the abscess after 28 days of therapy (**Table 11**)

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Surveillance Studies

Bryowsky et al (2023) evaluated the *in vitro* activity of cefiderocol against Enterobacterales isolates obtained in US hospitals between 2020–2022 as part of the SENTRY Antimicrobial Surveillance Program.[15]

Methods[15]

- Of the 11,805 Enterobacterales isolates collected, 9% (1015) originated from IAI sites. 6 isolates were identified as CRE and 62 were MDR Enterobacterales isolates
- CRE was defined as resistance to meropenem and imipenem. MDR Enterobacterales was defined as being NS to ≥1 antibiotic from ≥3 classes. XDR isolates were defined as being NS to ≥2 classes, according to 2022 CLSI criteria

Results[15]

- Cefiderocol demonstrated high activity against the CRE and MDR Enterobacterales isolates, originating from IAIs, with susceptibility ranging from 83.3–95.2%
- **Table 12** shows susceptibility rates to cefiderocol for the IAI pathogens

Table 12. Susceptibility for CRE and MDR Enterobacterales Isolates from IAIs According to CLSI[15]

Agent	Isolates Susceptible (%)		
	All Enterobacterales Isolates (n=10[illegible])	CRE Isolates (n=6)	MDR Enterobacterales Isolates (n=62)
Cefiderocol		83.3	95.2
Ceftazidime–avibactam		83.3	98.4
Ceftolozane–tazobactam		0	56.5
Imipenem–relebactam		83.3	98.4
Meropenem–vaborbactam	99.9	83.3	98.4

Nguyen et al (2023) evaluated the *in vitro* activity of cefiderocol against *P. aeruginosa* (n=3383), *A. baumannii-calcoaceticus* complex (n=910), and *S. maltophilia* (n=657) isolates by infection type from US hospitals in the SENTRY Antimicrobial Surveillance Program between 2020 and 2022.[16]

- The study included 198 IAI isolates from the following pathogens: *P. aeruginosa* (n=153), carbapenem-NS *P. aeruginosa* (n=21), *A. baumannii-calcoaceticus* complex (n=8), and *S. maltophilia* (n=16)
  - There were no carbapenem-NS *Acinetobacter* isolates for the IAI sites
- Cefiderocol susceptibility rates for the IAI pathogens can be found in **Table 13**

Table 13. Susceptibility for *P. aeruginosa*, *A. baumannii-calcoaceticus* complex, and *S. maltophilia* Isolates from IAIs According to CLSI[16]

Agent	Isolates Susceptible (%)		
	Carbapenem-NS *P. aeruginosa* (n=21)	*A. baumannii-calcoaceticus* complex Overall (n=6)	*S. maltophilia* (n=16)
Cefiderocol	100	100	100
Imipenem–relebactam	[illegible]		
Ceftazidime–avibactam		–	
Ceftolozane–tazobactam			
Meropenem		100	–
Imipenem		100	
Ampicillin–sulbactam		87.5	
Minocycline		100	100
Levofloxacin		–	62.5
Trimethoprim–sulfamethoxazole			93.8

Fetroja® – Use in Intraabdominal Infections (IAIs)

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Surveillance Studies

Table 12. Susceptibility for CRE and MDR Enterobacterales Isolates from IAIs According to CLSI[15,a]

Agent	Isolates Susceptible (%)		
	All Enterobacterales Isolates (n=1015)	CRE Isolates (n=6)	MDR Enterobacterales Isolates (n=62)
Cefiderocol	99.5	83.3	95.2
Ceftazidime–avibactam	99.8	83.3	98.4
Ceftolozane–tazobactam	92.8	0	56.5
Imipenem–relebactam	97	83.3	98.4
Meropenem–vaborbactam	99.9	83.3	98.4

Abbreviations: CLSI, Clinical and Laboratory Standards Institute; CRE, carbapenem-resistant Enterobacterales; MDR, multi-drug resistant.
[a]CLSI interpretive breakpoints for cefiderocol against Enterobacterales: susceptible, MIC ≤4 µg/mL; intermediate, MIC=8 µg/mL; resistant, MIC ≥16 µg/mL.
Table adapted from Bryowsky et al. IDWeek. 2023.

- The study included 198 IAI isolates from the following pathogens: *P. aeruginosa* (n=153), carbapenem-NS *P. aeruginosa* (n=21), *A. baumannii-calcoaceticus* complex (n=8), and *S. maltophilia* (n=16)
  - There were no carbapenem-NS *Acinetobacter* isolates for the IAI sites
- Cefiderocol susceptibility rates for the IAI pathogens can be found in **Table 13**

Table 13. Susceptibility for *P. aeruginosa*, *A. baumannii-calcoaceticus* complex, and *S. maltophilia* Isolates from IAIs According to CLSI[16]

Surveillance Studies

Table 13. Susceptibility for *P. aeruginosa*, *A. baumannii-calcoaceticus* complex, and *S. maltophilia* Isolates from IAIs According to CLSI[16,a,b]

Agent	Isolates Susceptible (%)		
	Carbapenem-NS *P. aeruginosa* (n=21)	*A. baumannii-calcoaceticus* complex Overall (n=6)	*S. maltophilia* (n=16)
Cefiderocol	100	100	100
Imipenem–relebactam	95.2	–	–
Ceftazidime–avibactam	90.5		
Ceftolozane–tazobactam	100		
Meropenem	–	100	
Imipenem		100	
Ampicillin–sulbactam		87.5	
Minocycline		100	100
Levofloxacin		–	62.5
Trimethoprim–sulfamethoxazole			93.8

Abbreviations: CLSI, Clinical and Laboratory Standards Institute; NS, non-susceptible.
[a]CLSI interpretive breakpoints for cefiderocol against *P. aeruginosa* and *A. baumannii* complex: susceptible, MIC ≤4 µg/mL; intermediate, MIC=8 µg/mL; resistant, MIC ≥16 µg/mL.
[b]CLSI interpretive breakpoints for cefiderocol against *S. maltophilia*: susceptible, MIC ≤1 µg/mL.
Table adapted from Nguyen et al. IDWeek. 2023.

can be found in **Table 13**

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Relevant Prescribing Information

Fetroja® is indicated in patients 18 years of age or older for the treatment of:[17]

- Complicated urinary tract infections (cUTIs), including pyelonephritis caused by the following susceptible Gram-negative microorganisms:
  - *Escherichia coli*
  - *Klebsiella pneumoniae*
  - *Proteus mirabilis*
  - *Pseudomonas aeruginosa*
  - *Enterobacter cloacae* complex
- Hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP), caused by the following susceptible Gram-negative microorganisms:
  - *Acinetobacter baumannii* complex
  - *Escherichia coli*
  - *Enterobacter cloacae* complex
  - *Klebsiella pneumoniae*
  - *Pseudomonas aeruginosa*
  - *Serratia marcescens*

Fetroja is contraindicated in:[17]

- Patients with a known history of severe hypersensitivity to cefiderocol or other beta-lactam antibacterial drugs, or any other component of **Fetroja**

Please read the attached **Fetroja Full Prescribing Information**

Literature Search

As of November 2025, a computerized search of the published medical literature using internal and external databases (ie, PubMed®, Medline® and Embase®) has identified additional relevant references regarding cefiderocol use in IAIs. For your review, these references are listed in the bibliography that follows:

- Tarski I, Śmiechowicz J, Duszyńska W. Cefiderocol in the successful treatment of complicated hospital-acquired *K. pneumoniae* NDM, OXA48 intraabdominal infection. *Infect Drug Resist*. 2024:17:5163-5170. [Web Link]
- Karruli A, Massa A, Andini R, et al. Clinical efficacy and safety of cefiderocol for resistant Gram-negative infections: a real-life, single-centre experience. *Int J Antimicrob Agents*. 2023;61(2):106723. [Web Link]
- Bleibtreu A, Dortet L, Bonnin RA, et al. Susceptibility testing is key for the success of cefiderocol treatment: a retrospective cohort study. *Microorganisms.* 2021;9(2):282. [Web Link]
- Contreras DA, Fitzwater SP, Nanayakkara DD, et al. Coinfections of two strains of NDM-1- and OXA-232-coproducing *Klebsiella pneumoniae* in a kidney transplant patient. *Antimicrob Agents Chemother.* 2020;64(4):e00948-19. [Web Link]

Please keep in mind that medical literature databases, while considered a major source of biomedical information, are selective in their sources, and the information derived from them should not be considered all-inclusive.

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Abbreviations

ACM	all-cause mortality	CRP	C-reactive protein
ADR	adverse drug reaction	CRRT	continuous renal replacement therapy
AE	adverse event	CST	colistin
AMK	amikacin	cUTI	complicated urinary tract infection
APACHE	acute physiology and chronic health evaluation	CVVH	continuous venovenous hemofiltration
ATM	aztreonam	CZA	ceftazidime–avibactam
BJI	bone and joint infection	C/T	ceftolozane–tazobactam
BSI	bloodstream infection	DAP	daptomycin
CC	clinical cure	DTR	difficult-to-treat resistant
CCI	Charlson Comorbidity Index	DTR-P	difficult-to-treat *P. aeruginosa*
CF	clinical failure	EAP	Early Access Program
CI	confidence interval	ECMO	extracorporeal membrane oxygenation
cIAI	complicated intraabdominal infection	EOT	end of treatment
CIP	ciprofloxacin	EUCAST	European Committee on Antimicrobial Susceptibility Testing
CLSI	Clinical and Laboratory Standards Institute	F	female
COPD	chronic obstructive pulmonary disease	FDA	US Food and Drug Administration
COVID-19	coronavirus disease 2019	FOS	fosfomycin
CR	carbapenem-resistant	g	grams
CRAB	carbapenem-resistant *A. baumannii*	h	hours
CRE	carbapenem-resistance Enterobacterales	HABP	hospital-acquired bacterial pneumonia
CR-Kp	carbapenem-resistant *K. pneumoniae*	HBV	hepatitis B virus
CRM	carbapenem resistance mechanism	HCC	hepatocellular carcinoma

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Abbreviations (Cont.)

HR	hazard ratio	q8h	every 8 hours
IAI	intraabdominal infection	q12h	every 12 hours
ICU	intensive care unit	RIF	rifampicin
IL	interleukin	RTI	respiratory tract infection
IQR	interquartile range	SAE	serious adverse event
IV	intravenous	SSSI	skin and skin structure infection
M	male	SSTI	skin and soft tissue infection
MC	microbiological cure	SOFA	Sequential Organ Failure Assessment
MDR	multidrug-resistant	TGC	tigecycline
MEM	meropenem	TID	three times a day
MIC	minimum inhibitory concentration	US	United States
NA	not available	UTI	urinary tract infection
NS	non-susceptible	VABP	ventilator-associated bacterial pneumonia
PCT	procalcitonin	VIM	Verona integron-encoded metallo-β-lactamase
PD	pharmacodynamic	XDR	extensively drug-resistant
PK	pharmacokinetic	ZD	zone diameter
Q	quartile		

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17. Fetroja® (cefiderocol) for injection, for intravenous use [Prescribing Information]. Shionogi Inc.

Enclosure

Fetroja® (cefiderocol) for injection, for intravenous use [Prescribing Information]. Shionogi Inc.