Fetroja® – Real-World Evidence

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Real-World Evidence in the US

Chou et al (2023) performed a prospective, real-world observational study evaluating clinical and microbiological outcomes in 48 patients receiving cefiderocol within the VHA system.[1]

- Clinical failure occurred in 17 (35.4%) patients, among whom 15 died within 72 h of failure
- The 30-day and 90-day ACM rates were 27.1% and 45.8%, respectively

El Ghali et al (2024) conducted a multicenter, retrospective study of 112 patients receiving ≥72 h of cefiderocol from 6 US medical centers between January 2018 and May 2023. The primary outcome was a composite of clinical success.[2]

- In the overall population, clinical success occurred in 69 (68.8%) patients, 30-day mortality in 18 (16.1%) patients, 30-day microbiologic recurrence in 16 (14.3%) patients, and clinical worsening in 16 (14.3%) patients

Gavaghan et al (2023) retrospectively assessed the real-world utilization and clinical outcomes in 24 patients treated with cefiderocol for ≥5 days as definite treatment for CR Gram-negative bacterial infections between October 2020 and September 2021. The median age was 66.5 years, and most patients (67%) were from a skilled nursing facility.[3]

- Clinical success was achieved in 11 (46%) patients and 10 patients (42%) died within 30 days

Real-World Evidence Outside the US

Giacobbe et al (2024) described the results of an interim pre-planned analysis of 200 patients from the CEFI-SITA study, an ongoing, multicenter, prospective study in Italy. The primary aim was to describe real-world use of cefiderocol in consecutive patients between August 2022 and September 2023.[4,5]

- Of the 145 patients receiving targeted cefiderocol therapy, the cumulative 30-day mortalities for Enterobacterales, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and MBL producers were 19.8%, 45%, 20.7%, and 22.7%, respectively

Soueges et al (2025) conducted a retrospective study in 114 immunocompromised adult patients who received cefiderocol from 12 French university hospitals between June 2020 and November 2023. The primary endpoints, assessed at Day 28, included infection cure, relapse, and overall/attributable mortality.[6]

- At Day 28, infection cure was achieved in 61 (53.3%) patients, relapse occurred in 20 (17.5%) patients, attributable mortality occurred in 29 (25.4%) patients, and overall mortality in 43 (37.7%) patients

Karruli et al (2023) performed a retrospective cohort study in 28 patients treated with cefiderocol in a single center in Italy. Clinical cure was achieved in 6 patients at Day 7 and 7 patients at Day 14. Clinical failure occurred in 6 patients and 9 patients at Day 7 and Day 14, respectively.[7]

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Real-World Evidence Outside the US (Cont.)

Palermo et al (2023) conducted a retrospective cohort study in 41 patients treated with cefiderocol for CR infection at a single center in Italy. Clinical cure was achieved at EOT in 23 (56.1%) patients. The 30-day ACM and in-hospital mortality rates were 36.6% and 46.3%, respectively.[8]

- AEs of maculopapular rash and bronchospasm occurred in 2 (4.9%) patients

Piccica et al (2023) evaluated a retrospective cohort of 142 patients treated with cefiderocol for CR infections at 3 centers in Italy. Overall, 30-day ACM occurred in 52 (37%) patients and there were no statistically significant differences in 30-day ACM by infection type. 8 patients experienced clinical and microbiological relapse 11 days after cefiderocol discontinuation.[9]

Giannella et al (2023) retrospectively assessed a cohort of 147 patients treated with cefiderocol for CR *Acinetobacter* spp. across 4 European countries. The overall clinical success rate was 53.1%, with a survival rate at Day 28 of 44.9%.[10]

Retrospective Comparative Studies

Larcher et al (2022) performed a retrospective observational cohort study in 27 patients (30 treatment courses) who received ≥72 h of treatment with cefiderocol, ceftazidime–avibactam–aztreonam, or imipenem–relebactam at Nimes University Hospital in France.[11]

- The infection-free survival rates for cefiderocol, ceftazidime-avibactam-aztreonam, and imipenem-relebactam were 48% (95% CI, 10.4–73.5), 33.3% (95% CI, 6.7–100), and 66.7% (95% CI, 30–100), respectively
- AEs occurred in 3 (13%) patients who received cefiderocol (eosinophilia, diarrhea, and hepatitis) and 1 patient (33.3%) who received imipenem–relebactam (eosinophilia)

Falcone et al (2022) conducted an observational retrospective cohort study comparing outcomes of patients with CRAB infections. Of the 124 patients included in the study, 47 (37.9%) received cefiderocol-based regimens and 77 (62.1%) received colistin-based regimens.[12]

- The 30-day ACM was lower in patients who received cefiderocol-based regimens (34%) compared to those who received colistin-based regimens (55.8%)

Pascale et al (2021) conducted a retrospective, multicenter, observational cohort study at 4 hospitals in Italy from January 2020 to April 2021. Of the 107 adult patients admitted to the ICU with severe COVID-19 and CRAB infections, 42 (39%) patients were treated with cefiderocol and 65 (61%) with colistin-based therapies. There was no significant difference in outcomes between the cefiderocol and colistin-based groups.[13]

- The mortality rate at Day 28 was 55% in patients receiving cefiderocol and 58% in patients receiving colistin-based regimens, respectively (P=0.706)

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Narrative and Systematic Review of Published Case Series/Case Reports

Wicky et al (2023) described the real-life experience of 16 patients treated with cefiderocol in the ICU for DTR non-fermenter infections at a single center in France between July 2020 and November 2021. Clinical failure and in-hospital mortality occurred in 6 (37.5%), and 5 (31.3%) patients, respectively.[14]

Viale et al (2022) performed a systematic literature review of published case reports and case series to evaluate the real-world experience of cefiderocol through either compassionate use or an expanded access program. Of the patients with available outcomes, clinical cure and eradication was reported in 80% and 72% of patients, respectively. The overall ACM rate was 35%.[15]

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Real-World Evidence in the US

Chou et al (2023) conducted a prospective, real-world observational study in patients (N=48) receiving cefiderocol for *P. aeruginosa* and other MDR Gram-negative infections within the VHA from 2019–2022. The study included patients admitted to acute- or long-term care VHA facilities who received at least 2 days of cefiderocol treatment.[1]

- Clinical outcomes included ACM, clinical failure, measured by a composite outcome of death or presence of signs or symptoms of infection, and microbiological failure, measured by culturing the same microorganism within 7 days of starting cefiderocol

Results[1]

- Among the 48 patients included in the study, the median (IQR) age and CCI was 70.5 years (60.5–74) and 6 (3–9), respectively
- The most common pathogens identified were *P. aeruginosa* (n=30, 62.5%), Enterobacterales (n=17, 35.4%), and *A. baumannii* (n=10, 20.8%). The most frequent sites of infection were lower respiratory tract (n=23, 47.9%), urinary tract (n=14, 29.2%), endovascular (n=9, 18.8%), and bone (n=4, 8.3%) infections
- Clinical failure occurred in 17 (35.4%) patients among whom 15 died within 72 h of failure. The 30-day and 90-day ACM rates were 27.1% and 45.8%, respectively
  - Clinical failure was highest in patients with intra-abdominal (1 [100%]) and endovascular (3 [42.9%]) infections
- Microbiologic failure at 30 and 90 days occurred in 14 (29.2%) and 20 (41.7%) patients, respectively
  - Microbiologic failure at 30 days was highest in patients with LRTI (7 [43.8%]), ≥2 infection sites (4 [44.4%]), and endovascular infection (3 [43.8%])
- The clinical and microbiological outcomes by *P. aeruginosa*, Enterobacterales, and *A. baumannii* infections are summarized in **Table 1**

Table 1. Clinical and Microbiological Outcomes in Patients Treated with Cefiderocol by Most Common Organisms[1]

Organism, n/N (%)	Clinical Failure	30-day ACM	90-day ACM	30-day Microbiologic Failure	90-day Microbiologic Failure
P. aeruginosa	6/18 (33.3)	4/18 (22.2)	8/18 (44.4)	6/18 (33.3)	8/18 (44.4)
Enterobacterales	3/8 (37.5)	3/8 (37.5)	4/8 (50)	0/8 (0)	2/8 (25)
A. baumannii	1/2 (50)	1/2 (50)	1/2 (50)	1/2 (50)	1/2 (50)

Abbreviation: ACM, all-cause mortality.
Table adapted from Chou et al. *Antimicrob Steward Healthc Epidemiol*. 2023.

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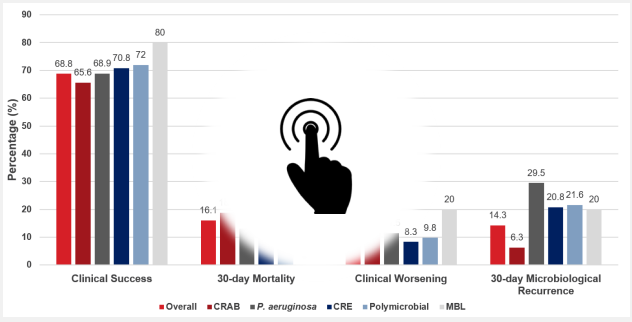
Real-World Evidence in the US (Cont.)

El Ghali et al (2024) performed a retrospective analysis of real-world data in 112 adults who received ≥72 h of cefiderocol treatment from 6 US medical centers between January 2018 and May 2023. The primary outcome was a composite of clinical success, including resolution of signs and symptoms, and survival and absence of symptomatic microbiologic recurrence at 30 days following treatment initiation.[2]

Results[2]

- The most common comorbidities included diabetes (37.5%), immunocompromised conditions (22.3%), and moderate to severe CKD (22.3%)
- Of the 112 patients enrolled, 110 (98.2%) had a CR infection
- The most common bacteria isolated were:
  - *P. aeruginosa* in 61 (54.5%) patients, of which 55 (90.2%) were CR
  - *A. baumannii* in 32 (28.6%) patients, of which all 32 were CR
  - *Klebsiella pneumoniae* in 15 (13.4%) of patients, of which 8 (53.3%) were CR
  - Polymicrobial infections were identified in 51 (45.5%) patients
- Of the 19 patients who underwent testing, 10 (52.6%) were identified as having an MBL (9 of which were NDM, and 1 VIM)
- LRTIs, including VABP (31.3%) and HABP (14.3%), were the most common infection sites, followed by SSTIs (18.8%), and IAIs (10.7%)
- 65.2% of patients received cefiderocol monotherapy and the median (IQR) duration of treatment was 9 (6–13) days
- In the overall population, 30-day mortality occurred in 18/112 (16.1%) patients, 30-day microbiologic recurrence in 16/112 (14.3%) patients, and clinical worsening in 16 (14.3%) patients
- Outcomes by pathogen are presented in **Figure 1**

Figure 1. Clinical Outcomes by Pathogen[2]



- Clinical success was achieved in 48/73 (65.8%) patients receiving cefiderocol monotherapy and 21/39 (53.8%) patients receiving combination therapy

Safety[2]

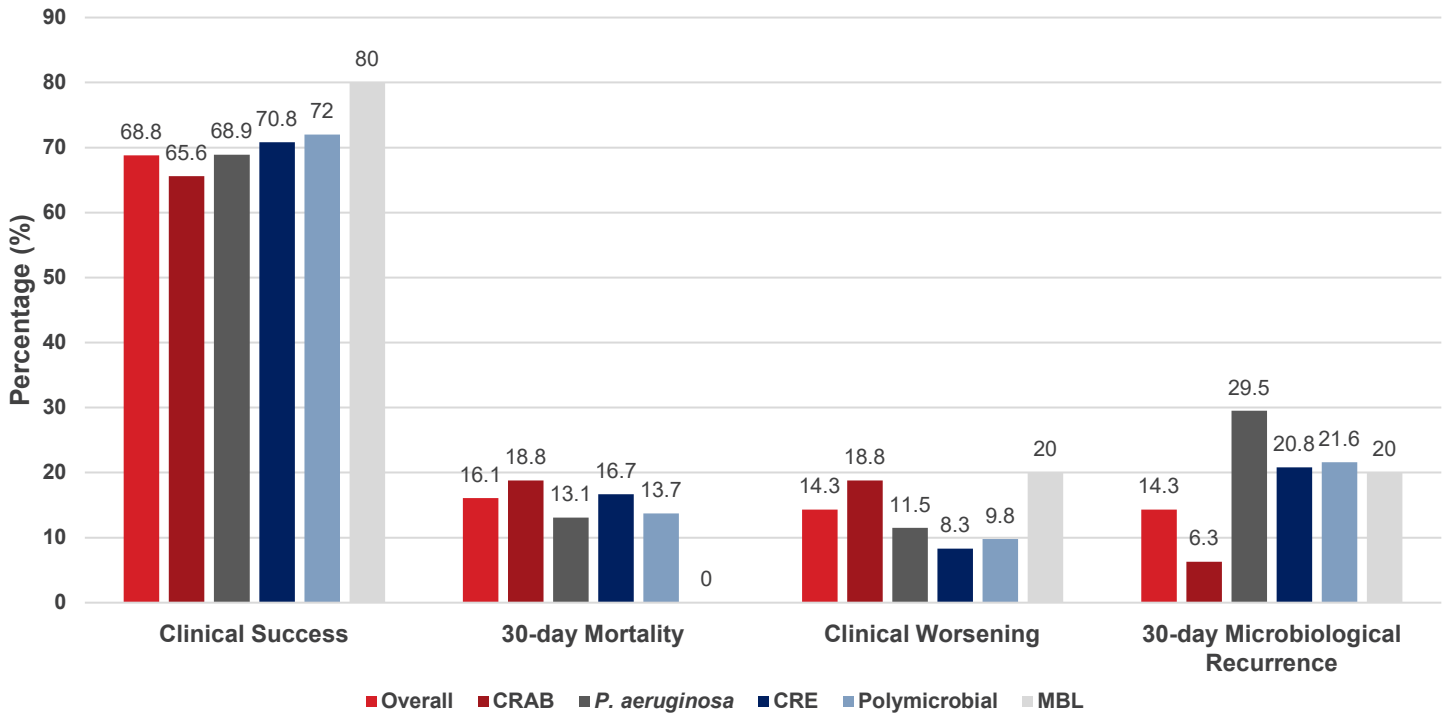
- 2 patients, both with a history of allergies to penicillin, developed a non-anaphylactic rash during cefiderocol treatment
- 17 patients with a history of β-lactam allergy, ranging from hives and itching to anaphylaxis and angioedema, received cefiderocol and experienced no allergic reactions during treatment

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Real-World Evidence in the US (Cont.)

Figure 1. Clinical Outcomes by Pathogen[2]



Abbreviations: CRAB, carbapenem-resistant *A. baumannii*; CRE, carbapenem-resistant Enterobacterales; MBL, metallo-β-lactamase.
Figure adapted from El Ghali et al. *Microbiol Spectr*. 2024.

(14.3%) patients, and clinical worsening in 16 (14.3%) patients

- Outcomes by pathogen can be found in **Figure 1**
- Clinical success was achieved in 48/73 (65.8%) patients receiving cefiderocol monotherapy and 21/39 (53.8%) patients receiving combination therapy

Safety[2]

- 2 patients, both with a history of allergies to penicillin, developed a non-anaphylactic rash during cefiderocol treatment
- 17 patients with a history of β-lactam allergy, ranging from hives and itching to anaphylaxis and angioedema, received cefiderocol and experienced no allergic reactions during treatment

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Real-World Evidence in the US (Cont.)

Gavaghan et al (2023) retrospectively assessed the real-world utilization and clinical outcomes in adult patients (N=24) who were treated with cefiderocol for at least 5 days as definite treatment for CR Gram-negative bacterial infections between October 2020 and September 2021. Clinical success was defined as the composite of survival at Day 30 and resolution of signs and symptoms of infection and absence of recurrence of infection at Day 30 due to the same bacterial species.[3]

- Cefiderocol susceptibility was determined based on US FDA interpretive criteria

Results[3]

- Of the 24 patients:
  - 14 (58%) had a history of CR pathogen in the prior 90 days
  - The infection types were pneumonia in 19 (79%) patients, wound infection in 4 (17%) patients, and either cUTI or driveline infections (1 patient [4%] each)
  - Concomitant bacteremia was found in 5 (21%) patients
- The most common pathogens were *A. baumannii* (58%), *P. aeruginosa* (42%), *K. pneumoniae* (17%), and *Stenotrophomonas maltophilia* (8%)
- Cefiderocol was administered as monotherapy in 16 (67%) patients and as part of combination therapy in 8 (33%), with colistin, gentamicin, minocycline, tigecycline, or tobramycin
- Clinical success was documented in 11 (46%) patients and 13 (54%) patients had clinical failure
- 10 patients (42%) died within 30 days:
  - 50% of the mortality cases received cefiderocol as monotherapy and 50% received cefiderocol combination therapy
  - Resistance was confirmed in 1 patient (10%)
  - Deaths were seen in 6 (60%) patients with *A. baumannii* infection and in 3 (3%) with *P. aeruginosa* infections
- Recurrence with the same pathogen occurred in 7 (29%) patients
- 2 patients demonstrated increased cefiderocol MIC values during repeat susceptibility testing (MICs of 2 and 32 µg/mL)
- No AEs were seen during cefiderocol treatment

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Real-World Evidence Outside the US

Giacobbe et al (2024) described an interim pre-planned analysis of 200 patients from the ongoing multicenter prospective CEFI-SITA study in Italy. The primary aim of this study was to describe the real-world use of cefiderocol in terms of indication, type of therapy, and clinical characteristics in consecutive patients between August 2022 and September 2023. Secondary objectives included clinical cure rates and 30-day mortality, and factors associated with the use of combination therapy versus monotherapy.[4]

Results[4,5]

- The most frequent comorbidities were diabetes (17.6%), CKD (16.2%), and solid neoplasm (14.7%)
- Cefiderocol was used as monotherapy in 101 (50.5%) cases and as combination therapy in 99 (49.5%) cases
  - Based on the results of multivariable models, previous isolation of CRAB and previous HSCT were the factors most associated with the use of cefiderocol as combination therapy
- Cefiderocol was administered as targeted therapy in 145 (72.5%) patients, and as empirical therapy in 55 (27.5%) patients
- Among patients receiving targeted therapy, the most common sites of infections were LRTIs (43.4%) and BSIs (38.6%). Among patients receiving empirical therapy, the most common sites of infection were sepsis (65.5%) and LRTIs (18.2%)
- Of the 145 evaluable monomicrobial infections, the most frequent pathogens were *A. baumannii* (54.9%), *P. aeruginosa* (20.5%), and *K. pneumoniae* (14.8%)
  - CR was identified in 57/62 (91.9%), 21/22 (95.5%), and 15/16 (93.8%) tested isolates for *A. baumannii*, *P. aeruginosa*, and *K. pneumoniae*, respectively
- The cumulative 30-day mortalities in patients receiving targeted therapy were 19.8% (95% CI, 7–37.4) for Enterobacterales, 45% (95% CI, 32.4–56.8) for *A. baumannii*, 20.7% (95% CI, 7.3–38.7) for *P. aeruginosa*, and 22.7% (95% CI, 8–41.9) for MBL-producing Gram-negative bacteria
- For patients receiving targeted therapy, the clinical outcomes by pathogen and mode of therapy are summarized in **Table 2**

Table 2. Clinical Outcomes for Patients Receiving Targeted Cefiderocol Monotherapy versus Combination Therapy[4,5]

Infection[a], n/N (%)	Outcomes			
	7-day Clinical Cure	14-day Clinical Cure	28-day Clinical Cure	Adjusted 28-day Clinical Cure[b]
Enterobacterales[c,e]	17/26 (65		17/23 (74)	20/26 (77)
Monotherapy	11/		10/12 (83)	12/14 (86)
Combination therapy[d]			7/11 (64)	8/12 (67)
P. aeruginosa[c,f]			19/23 (83)	21/25 (84)
Monotherapy			10/12 (83)	12/14 (86)
Combination therapy[d]			9/11 (82)	9/11 (82)
A. baumannii[c,g]	3		25/55 (45)	35/65 (54)
Monotherapy	17/		15/27 (56)	17/29 (59)
Combination therapy[d]	18/36 (50		10/28 (36)	18/36 (50)
MBL-producing Gram-negative[c,h,i]	16/22 (73)	17/22 (77)	17/22 (77)	17/22 (77)
Monotherapy	10/13 (77)	11/13 (85)	11/13 (85)	11/13 (85)
Combination therapy[d]	6/9 (67)	6/9 (67)	6/9 (67)	6/9 (67)

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Real-World Evidence Outside the US

Table 2. Clinical Outcomes for Patients Receiving Targeted Cefiderocol Monotherapy versus Combination Therapy[4,5]

Infection[a], n/N (%)	Outcomes			
	7-day Clinical Cure	14-day Clinical Cure	28-day Clinical Cure	Adjusted 28-day Clinical Cure[b]
Enterobacterales[c,e]	17/26 (65)	18/25 (72)	17/23 (74)	20/26 (77)
Monotherapy	11/14 (79)	11/13 (85)	10/12 (83)	12/14 (86)
Combination therapy[d]	6/12 (50)	7/12 (58)	7/11 (64)	8/12 (67)
P. aeruginosa[c,f]	21/25 (84)	20/24 (83)	19/23 (83)	21/25 (84)
Monotherapy	12/14 (86)	11/13 (85)	10/12 (83)	12/14 (86)
Combination therapy[d]	9/11 (82)	9/11 (82)	9/11 (82)	9/11 (82)
A. baumannii[c,g]	35/65 (54)	32/61 (52)	25/55 (45)	35/65 (54)
Monotherapy	17/29 (59)	15/28 (54)	15/27 (56)	17/29 (59)
Combination therapy[d]	18/36 (50)	17/33 (52)	10/28 (36)	18/36 (50)
MBL-producing Gram-negative[c,h,i,j]	16/22 (73)	17/22 (77)	17/22 (77)	17/22 (77)
Monotherapy	10/13 (77)	11/13 (85)	11/13 (85)	11/13 (85)
Combination therapy[d]	6/9 (67)	6/9 (67)	6/9 (67)	6/9 (67)

Abbreviations: BJI, bone and joint infection; BSI, bloodstream infection; IAI, intra-abdominal infection; LRTI, lower respiratory tract infection; MBL, metallo-β-lactamase; SSTI, skin and soft tissue infection; UTI, urinary tract infection.
[a]Discharged patients excluded from denominator, with the exception of the sensitivity analysis for adjusted 28-day mortality. Missing information excluded from denominator. [b]Sensitivity analysis considering also discharged patients as clinically cured at Day 28. [c]Infection by only 1 Gram-negative genus (with the exception of Enterobacterales infection, for which concomitant infection by > 1 member of the Enterobacterales order was also considered). [d]Anti-CR-GNB combination was defined as treatment with cefiderocol in combination with at least 1 of the following agents: aminoglycosides; fosfomycin; tigecycline (with the exception of targeted therapy of *P. aeruginosa* infections); polymyxins; sulbactam or ampicillin–sulbactam (as empirical treatment of as targeted therapy for *A. baumannii* infections). [e]Site(s) of Enterobacterales infection: BSI (n=12); LRTI (n=7); UTI (n=2); SSTI (n=1); IAI (n=1); IAI plus BSI(n=1); LRTI plus BSI (n=1); UTI plus BSI infection (n=1). [f]Site(s) of *P. aeruginosa* infection (n=25): LRTI (n=12); BSI (n=6); UTI (n=2); BJI plus BSI (n=1); IAI (n=1); LRTI plus BSI (n=1); SSTI (n=1); SSTI plus BSI (n=1). [g]Site(s) of *A. baumannii* infection (n=67): LRTI (n=30); BSI (n=29); BJI (n=2); UTI (n=2); IAI (n=1); LRTI plus BSI (n=1); SSTI (n=1); site(s) not reported (n=1). [h]Site(s) of MBL-producing Gram-negative infection (n=22): LRTI (n=8); BSI (n=5); UTI (n=3); IAI (n=2); SSTI (n=2): LRTI plus BSI (n=1); SSTI plus BSI (n=1). [i]Type of MBL enzyme (n=20): NDM (n=12); VIM (n=19); NDM (n=3). [j]Type of MBL-producing causative agent: *P. aeruginosa* (n=12); Enterobacterales (n=10).
Table adapted from Giacobbe et al. *Infect Dis Ther*. 2024 (plus Supplementary Appendix).

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Real-World Evidence Outside the US (Cont.)

Soueges et al (2025) conducted a retrospective study in 114 immunocompromised adult patients who received cefiderocol from 12 French university hospitals between June 2020 and November 2023. The primary endpoints, assessed at Day 28, included infection cure, relapse, and overall/attributable mortality. Attributable mortality was defined as death related to the documented infection requiring cefiderocol treatment.[6]

Results[6]

- The most common immunocompromising conditions were hematological malignancy (38.5%), solid organ transplant (35%), active solid neoplasia (24.5%), and HSCT (16.6%)
- The most common infection sites treated were respiratory (48.2%), followed by urinary (14%), and IAIs (9.6%)
- The majority of infections were non-fermenters, with *P. aeruginosa* occurring the most in 51 (56%) patients, and of the 51 patients with *P. aeruginosa infections*, 8 (11.7%) were VIM producers
  - Other common pathogens included *S. maltophilia* (14.3%), Enterobacterales (12.1%), and CR OXA-23-producing *Acinetobacter* (6.6%)
- The median duration of cefiderocol was 10 days, and cefiderocol was used as monotherapy in 56 (49.1%) cases
- At Day 28:
  - Infection cure was achieved in 61 (53.3%) patients
  - Relapse occurred in 20 (17.5%) cases
  - Attributable mortality occurred in 29 (25.4%) patients and overall mortality in 43 (37.7%) patients
- At Day 90, attributable mortality occurred in 39 (35.1%) patients and overall mortality in 58/111 (52.2%, 3 lost to follow-up). Relapse occurred in 7 (9.8% of alive patients at Day 28)
- In multivariable analysis adjusted for septic shock, Day 28 overall mortality was significantly associated with BSIs and RTIs (aOR 4.12 [95% CI, 1.48–11.5], P=0.007, and aOR 8.04 [95% CI, 2.48–26.03], P<0.001, respectively)

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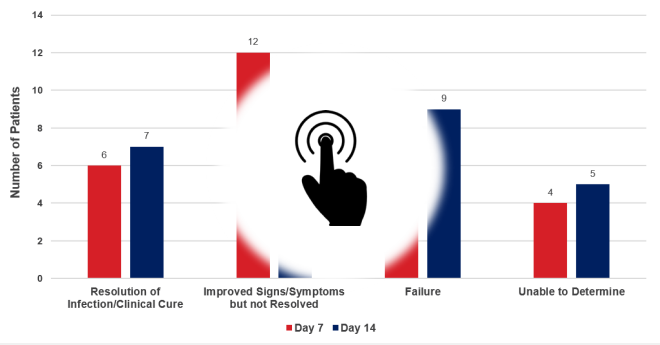
Real-World Evidence Outside the US (Cont.)

Karruli et al (2023) described a single-center retrospective study in Italy which assessed outcomes for 28 patients treated with cefiderocol. The primary outcome was patient status (alive or deceased) at hospital discharge. Secondary outcomes included treatment response at Days 7 and 14 (defined as resolution of the infection/clinical recovery, improvement of signs and symptoms without complete resolution, or therapeutic failure), microbiological eradication, and treatment tolerability.[7]

Results[7]

- Of the 28 patients included, 8 (28.6%) were given cefiderocol while in the ICU. The most common comorbidities included prior MI (39.2%), COPD, CKD and diabetes mellitus (28.6% each), and solid cancer (25%)
- The most common pathogens treated were *A. baumannii* (31.1%), *P. aeruginosa* (20%), and *S. maltophilia* (16%)
- The most common infection sites treated were respiratory (38%), followed by bloodstream (24.4%), and urinary (22%)
- 6 patients received combination therapy which included colistin (n=2), ceftazidime–avibactam (n=2), amikacin (n=2), tigecycline (n=1) or fosfomycin (n=1)
- Overall, 17 (60.7%) patients were alive at discharge; 11 (39.3%) had died
- Hospital mortality rates were not significantly different between patients treated with monotherapy (31.8%) versus combination therapy (66.6%), *P*=0.174
- The clinical outcomes at Day 7 and 14 are shown in **Figure 2**
- 1 AE (*Clostridioides difficile* colitis requiring discontinuation) was reported

Figure 2. Clinical Outcomes at Day 7 and Day 14 of Patients Treated with Cefiderocol (N=28)[7]



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Real-World Evidence Outside the US (Cont.)

Figure 2. Clinical Outcomes at Day 7 and Day 14 of Patients Treated with Cefiderocol (N=28)[7]

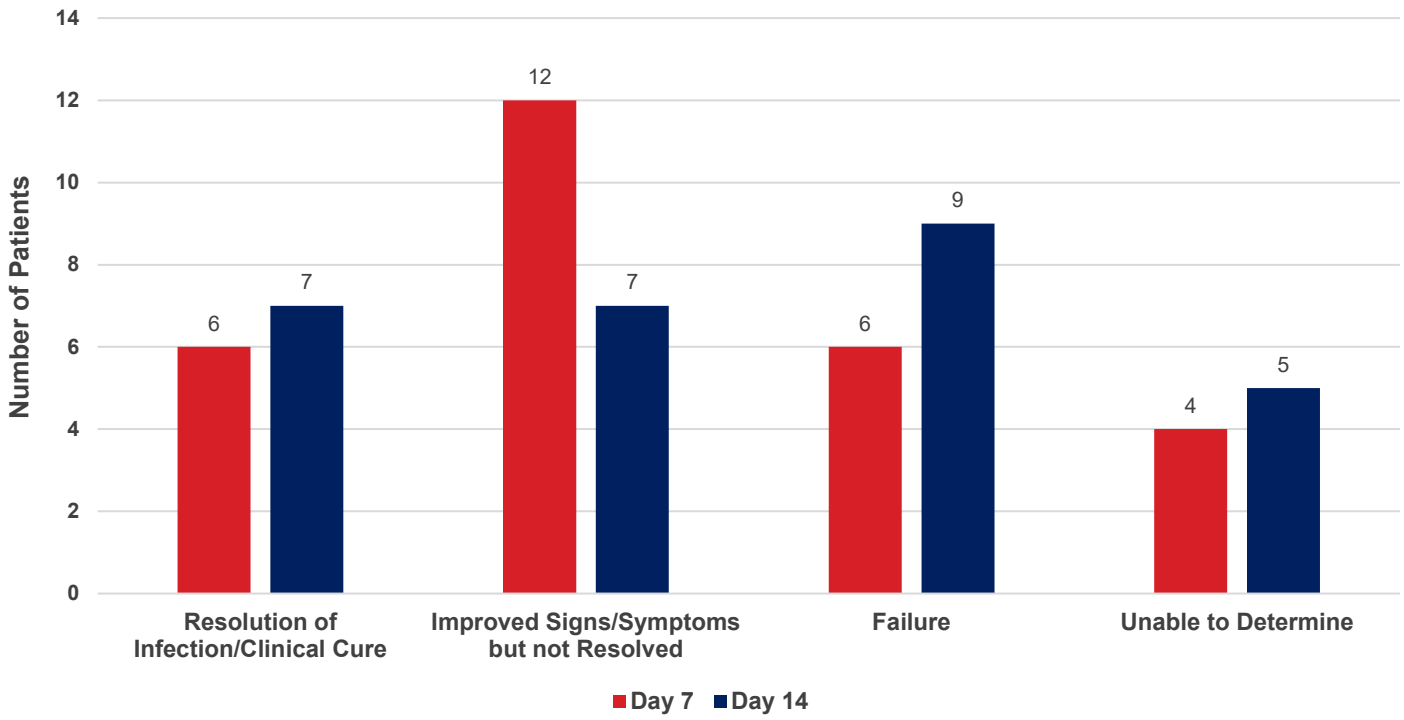


Figure adapted from Karruli et al. *Int J Antimicrob Agents*. 2023.

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Real-World Evidence Outside the US (Cont.)

Palermo et al (2023) performed a single-center, retrospective study which reported outcomes for 41 patients with CR infections treated with cefiderocol in Italy. The primary outcome was 30-day ACM and secondary outcomes included clinical response during the first 72 h of therapy (response in which a switch in therapy was not necessary or the patient did not die); clinical cure at EOT (resolution of symptoms and inflammatory markers); need to switch therapy (discontinuation of cefiderocol due to clinical or microbiological failure); and microbiological eradication (eradication of isolated pathogen at EOT).[8]

Results[8]

- Overall, 10 (24.4%) patients were treated with cefiderocol in combination with fosfomycin (n=6; 14.6%) or colistin (n=4; 9.6%)
- Patient characteristics for 30-day survivors and non-survivors are presented in **Table 3**

Table 3. Patient Characteristics Stratified by 30-day Survivors and Non-Survivors[8]

Characteristic	Study Population (N=41)	30-day Survivors (N=26)	30-day Non-Survivors (N=15)	*P* Value
Age, median (IQR) years Age >70	70 (54–75) 19 (46.3%)	60 (51–75) 8 (30.8%)	73 (70–78) 11 (73.3%)	0.02 0.008
CCI, median CCI ≥4	5 (3–6) 29 (70.7%)	4 (2–6) 15 (57.7%)	5 (5–6) 14 (93.3%)	0.07 0.01
Previous hospital admission within the past 12 months	20 (48.8%)	11 (42.3%)	9 (60%)	0.27
Treated in the ICU	13 (31.7%)	7 (26.9%)	6 (40%)	0.39
Common types of infections HABP cUTI cIAI SSTI	 17 (41.5%) 5 (12.2%) 8 (19.5%) 9 (21.9%)	 8 (30.8%) 5 (19.2%) 3 (11.5%) 8 (30.8%)	 9 (60%) 0 (0%) 5 (33.3%) 1 (6.7%)	 0.05 0.06 0.08 0.07
Common bacterial isolates *A. baumannii* *K. pneumoniae* *P. aeruginosa*	 31 (75.6%) 10 (24.4%) 5 (12.2%)	 20 (76.9%) 6 (23.1%) 2 (7.7%)	 11 (73.3%) 4 (26.7%) 3 (20%)	 0.79 0.79 0.41
Polymicrobial isolates	9 (22%)	6 (23.1%)	3 (20%)	0.47

Abbreviations: CCI, Charlson Comorbidity Index; cIAI, complicated intra-abdominal infection; cUTI, complicated urinary tract infection; HABP, hospital-acquired bacterial pneumonia; ICU, intensive care unit; IQR, interquartile range; SSTI, skin and soft tissue infection.
Table adapted from Palermo et al. *Antibiotics (Basel)*. 2023.

- Overall, the in-hospital mortality rate was 46.3%, and the 30-day ACM rate was 36.6%
- Microbiological eradication and clinical cure at EOT occurred in 33 (80.5%) and 23 (56.1%) patients
- AEs (maculopapular rash and bronchospasm) occurred in 2 (4.9%) patients

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Real-World Evidence Outside the US (Cont.)

Piccica et al (2023) held a retrospective study of 142 patients with CR infections to identify factors predictive of 30-day mortality. Patients in the study were adults (≥18 years) who received ≥3 days of cefiderocol treatment in 3 tertiary care centers in Italy. The primary outcome was 30-day mortality. Additionally, a propensity score analysis was performed to determine the efficacy of cefiderocol monotherapy versus combination therapy.[9]

Results[9]

- The most common pathogens identified were *A. baumannii* (62.7%), *P. aeruginosa* (19%), and *K. pneumoniae* (15.5%). Most common infection sites were LRTI (57%) and bacteremia (13.4%)
  - In total, 79 (55.6%) patients were in the ICU
- The overall 30-day ACM occurred in 52 (37%) patients
- By infection type there was no statistically significant difference in 30-day ACM. There was a numerically higher occurrence of deaths in LRTIs (43%), cUTIs (33%), acute bacterial skin and skin structure infections (33%), and IAIs (31%)
- After a median of 11 days post-cefiderocol discontinuation, 8 (6%) patients experienced a clinical and microbiological relapse
  - They received a second course of cefiderocol for a median of 12 days (IQR, 9–18 days)
- In the 72 (51%) patients who received cefiderocol combination therapy, the mortality rate was 40% compared with 33% in the 70 (49%) patients receiving monotherapy; there was no significant difference between groups with propensity score adjustments (IPTW-adjusted HR: 1.08, 95% CI, 0.61–1.92)
- There was no statistically significant difference in the major AEs, including acute respiratory distress syndrome, acute kidney injury, and septic shock

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Real-World Evidence Outside the US (Cont.)

Giannella et al (2023) conducted a retrospective, observational, descriptive cohort study (ARES) in 147 adult patients with CR *Acinetobacter* spp. infections between April 2020 and April 2021 across 4 European countries. Cefiderocol was obtained through the Early Access Program in Europe and initiated for at least 72 h in patients receiving cefiderocol for the first time. Clinical success, defined as a composite of clinical resolution of signs and symptoms of infection at Day 14, or survival at Day 28 following the initial dose of cefiderocol, was the primary outcome.[10]

- Secondary outcomes included clinical outcomes (resolution of signs and symptoms of infection and treatment failure at Day 7 and Day 14 and relapse of primary infection), survival at Day 14 and Day 28, and safety

Results[10]

- Overall, the clinical success rate was 53.1%, with 39.5% achieving resolution of infection at Day 14 and a survival rate of 44.9% at Day 28
- Polymicrobial, Gram-negative infections were present in 36 (24.5%) patients, with the most common co-infecting pathogens being *K. pneumoniae* (9.5%) and *P. aeruginosa* (6.8%)
  - Clinical success occurred in 20 (55.6%) patients with polymicrobial infections

Safety[10]

- Adverse drug reactions occurred in 7 (4.8%) patients with 2 (1.4%) patients experiencing 3 severe/serious adverse drug reactions (cardiac arrest, renal tubular necrosis, and tubulointerstitial nephritis)

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Retrospective Comparative Studies

Larcher et al (2022) conducted an observational cohort study from January 1, 2020, to August 31, 2022, in 27 patients (30 treatment courses) at Nimes University Hospital in France. Adult patients that were hospitalized and received ≥72 h of treatment with imipenem–cilastatin–relebactam, meropenem–vaborbactam, ceftazidime–avibactam–aztreonam, or cefiderocol during the outlined study period were included.[11]

- The primary objective was infection-free survival rate, defined as survival without recurrence of the infection. In addition, rates of microbiological cure, clinical cure, recurrent infection, AEs, and death were also recorded. Follow-up was up to 90 days

Results[11]

- LRTI (53%) was the most common reason for hospital admission, followed by COVID-19 (50%). Ceftazidime–avibactam–aztreonam was primarily used for NDM-1 producing *K. pneumoniae*, whereas cefiderocol and imipenem–cilastatin–relebactam were administered mostly for the treatment of DTR *P. aeruginosa*
- Overall, infection-free survival rates were:
  - Cefiderocol: 48% (95% CI, 10.4–73.5)
  - Ceftazidime–avibactam–aztreonam: 33.3% (95% CI, 6.7–100)
  - Imipenem–cilastatin–relebactam: 66.7% (95% CI, 30–100)
- Additional antimicrobial characteristics, and outcomes for cefiderocol, ceftazidime–avibactam–aztreonam, and imipenem–cilastatin–relebactam are listed in **Table 4**

Table 4. Antimicrobial Characteristics and Outcomes for Cefiderocol, Ceftazidime–Avibactam–Aztreonam, and Imipenem–Cilastatin–Relebactam[11]

	Cefiderocol (n=24)[a]	Ceftazidime–Avibactam –Aztreonam (n=3)	Imipenem–Cilastatin –Relebactam (n=3)
	n (%) or Median (IQR)		
Infection site			
Pneumonia	17 (71)	2 (67)	2 (67)
VABP	17 (71)	1 (33)	1 (33)
BSI	5 (21)	1 (33)	0
CR-BSI	3 (13)	1 (33)	0
BJI	2 (8)	0	1 (33)
IAI	2 (8)	1	0
UTI	1		0
Meningitis	1		0
Reason for antibiotic initiation			
DTR *P. aeruginosa*			3 (100)
NDM *K. pneumoniae*			0
Other			0
Antimicrobial therapy characteristics			
Duration (days)	14		42 (35–42)
Daily dose (grams)	6		2/1
Daily regimen	TID		QID
Infusion time (hours)	3 (3–4)	(2–7)	0.5 (0.5–0.5)
Combination therapy	13 (54)	3 (100)	2 (67)
Outcomes			
Death (all-cause)	5 (21)	2 (67)	0
Sepsis-related	3 (13)	1 (33)	0
WLS	2 (8)	1 (33)	0
Clinical failure	7 (29)	2 (66)	0
Microbiological failure	10 (42)	0	0
Recurrent infection	5 (21)	0	1 (33)
AE[a]	3 (13)	0	1 (33)

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Retrospective Comparative Studies

Table 4. Antimicrobial Characteristics and Outcomes for Cefiderocol, Ceftazidime–Avibactam–Aztreonam, and Imipenem–Cilastatin–Relebactam[11]

	Cefiderocol (n=24)[a]	Ceftazidime–Avibactam –Aztreonam (n=3)	Imipenem–Cilastatin –Relebactam (n=3)
	n (%) or Median (IQR)		
Infection site			
Pneumonia	17 (71)	2 (67)	2 (67)
VABP	17 (71)	1 (33)	1 (33)
BSI	5 (21)	1 (33)	0
CR-BSI	3 (13)	1 (33)	0
BJI	2 (8)	0	1 (33)
IAI	2 (8)	0	0
UTI	1 (4)	0	0
Meningitis	1 (4)	0	0
Reason for antibiotic initiation			
DTR *P. aeruginosa*	19 (79)	0	3 (100)
NDM *K. pneumoniae*	1 (4)	3 (100)	0
Other	6 (25)	1 (33)	0
Antimicrobial therapy characteristics			
Duration (days)	14 (12–31)	14 (12–18)	42 (35–42)
Daily dose (grams)	6 (24)	6/1.5/6	2/1
Daily regimen	TID	TID	QID
Infusion time (hours)	3 (3–4)	2 (2–7)	0.5 (0.5–0.5)
Combination therapy	13 (54)	3 (100)	2 (67)
Outcomes			
Death (all-cause)	5 (21)	2 (67)	0
Sepsis-related	3 (13)	1 (33)	0
WLS	2 (8)	1 (33)	0
Clinical failure	7 (29)	2 (66)	0
Microbiological failure	10 (42)	0	0
Recurrent infection	5 (21)	0	1 (33)
AE[a]	3 (13)	0	1 (33)

Abbreviations: AE, adverse event; BJI, bone and joint infection; BSI, bloodstream infection; CR-BSI, catheter-related bloodstream infection; DTR, difficult-to-treat resistant; IAI, intra-abdominal infection; IQR, interquartile range; NDM, New Delhi metallo-β-lactamase; QID, once a day; TID, three times a day; UTI, urinary tract infection; WLS, withdrawal of life support; VABP, ventilator-associated bacterial pneumonia.
[a]Details of AEs, eosinophilia (cefiderocol n=1, imipenem–relebactam n=1), diarrhea (cefiderocol n=1), hepatitis (cefiderocol n=1).
Table adapted from Larcher et al. *Front Cell Infect Microbiol*. 2022.

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Retrospective Comparative Studies (Cont.)

Falcone et al (2022) completed an observational retrospective cohort study in 124 patients with CRAB infections receiving cefiderocol (n=47) or colistin-based regimens (n=77) for at least 48 h. Patients included were consecutively hospitalized at the University Hospital of Pisa in Italy between June 2019 and August 2021.[12]

- The primary objective was to study 30-day ACM (death within 30 days of CRAB infection) in cefiderocol versus colistin-based regimens. Secondary endpoints included the occurrence of AEs during the antibiotic treatment and microbiological failure, defined as CRAB from the same infection site, isolated ≥7 days after the end of treatment
- Cefiderocol 2 g q8h was administered as a 3 h IV infusion and adjusted for renal dosing if needed. Patients received cefiderocol as monotherapy (n=15) or in combination with other antibiotics (n=32) based on clinical judgment
- Colistin was given at a loading dose of 9 million IU followed by 4.5 million IU q12h and administered with other antibiotics based on clinical judgment

Results[12]

- Infections were classified as BSI (n=79), VABP (n=35), and others (n=10)
- The 30-day ACM for the cefiderocol group was 34%, and 55.8% in the colistin group (*P*=0.018). In addition, a subgroup analysis in patients with BSI and VABP was conducted for mortality at 14 days and 30 days (**Figure 3**)
- The multivariable analysis results are presented in **Table 5**. The results showed that cefiderocol (compared to colistin-based regimens) was seen as a protective factor for 30-day mortality (aHR 0.32, 95% CI, 0.18–0.57; *P*<0.001)

Microbiological Failure and Resistance[12]

- Microbiological failure rates were calculated in patients that had available follow-up cultures (120/124)
- The difference in microbiological failure between the 2 groups was not statistically significant (*P*=0.079), with failure in 8/46 (17.4%) patients in the cefiderocol group and 5/74 (6.8%) patients in the colistin group
- All of the patients experiencing failure had BSI, and 6 of these patients received cefiderocol monotherapy. Microbiological failure was significantly higher in patients treated with monotherapy versus combination therapy, 42.9% versus 6.3%, respectively (*P*=0.006)

Safety[12]

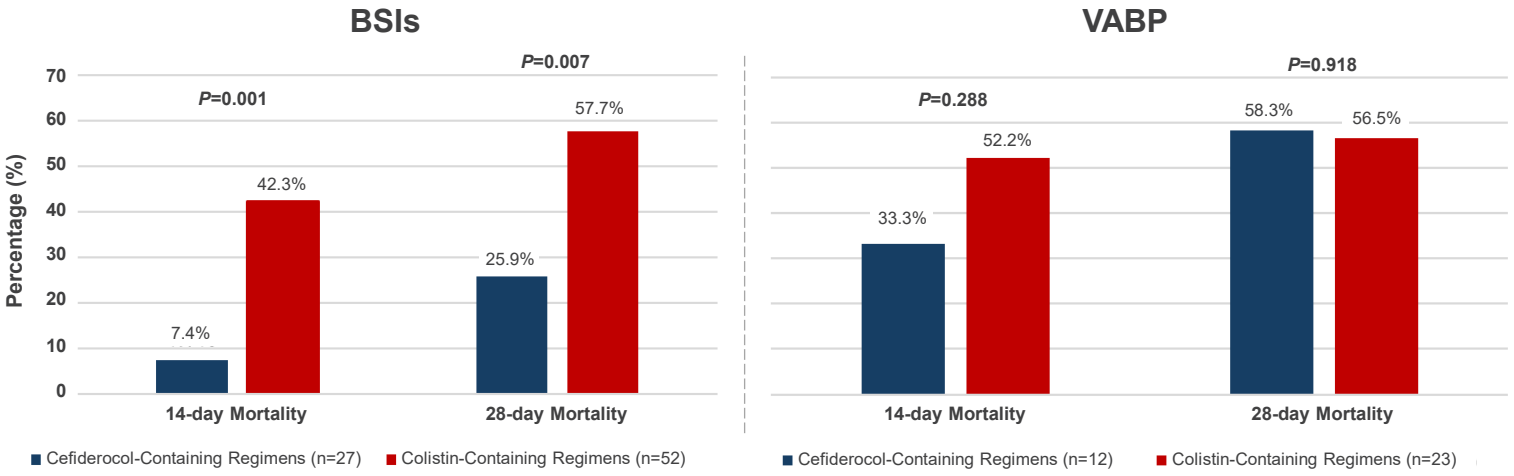
- An AE occurred in 1 (2.1%) patient treated with cefiderocol and in 16 (21.1%) patients treated with colistin-based regimens (*P*=0.003). All patients experiencing an AE in the colistin-based group reported acute kidney injury during treatment. The AE reported for cefiderocol was skin rash

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Retrospective Comparative Studies (Cont.)

Figure 3. 14- and 30-day Mortality in Patients with BSI and VABP[12]



Abbreviations: BSI, bloodstream infection; VABP, ventilator-associated bacterial pneumonia.
Figure adapted from Falcone et al. *Antimicrob Agents Chemother*. 2022.

Table 5. Cox Regression Multivariable Analysis of Factors Independently Associated with 30-day Mortality[12]

Analysis and Factor	aHR (95% CI)	*P* Value[a]
Cox regression multivariable analysis		
Septic shock	2.56 (1.11–5.94)	0.028
SOFA score	1.15 (1.05–1.27)	0.003
Age	1.05 (1.02–1.07)	0.001
Cefiderocol-containing regimens[b] (colistin-containing regimens[c] as reference variable)	0.32 (0.18–0.57)	<0.001
Propensity score analysis		
Cefiderocol-containing regimens[b] (IPTW-adjusted)	0.44 (0.22–0.66)	<0.001

Abbreviations: aHR, adjusted hazard ratio; CI, confidence interval; IPTW, inverse probability of treatment weighting; SOFA, Sequential Organ Failure Assessment.
[a]Statistically significant is $P<0.05$.
[b]Cefiderocol as monotherapy or in combination with tigecycline, fosfomycin, ertapenem, ampicillin–sulbactam, or meropenem–vaborbactam.
[c]Colistin alone or in combination with tigecycline, meropenem, rifampin, fosfomycin, aminoglycosides, or ampicillin–sulbactam.
Table adapted from Falcone et al. *Antimicrob Agents Chemother*. 2022.

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Retrospective Comparative Studies (Cont.)

Pascale et al (2021) conducted a retrospective, multicenter, blinded, cohort study in Italy for adult patients with COVID-19 and CRAB co-infections that were admitted to the ICU between January 2020 and April 2021. Cefiderocol was obtained through the Early Access program and administered at the standard dose (2 g q8h) with adjustments for kidney function.[13]

- The primary endpoint was ACM at Day 28 following the diagnosis of CRAB infection. Secondary endpoints included clinical cure (ie, resolution of fever and hypotension) at Day 14, microbiological cure (ie, clearance of bacteria from follow-up blood samples or respiratory samples) at Day 14

Results[13]

- A total of 107 patients were included in the analysis (42 patients were treated with cefiderocol monotherapy and 65 patients were treated with colistin, mostly as part of a combination regimen)
- LRTI was diagnosed in 44 (41%) and BSI was diagnosed in 62 (58%) patients
- Septic shock was present in 43 (41%) patients: cefiderocol 18 (46%) and colistin 25 (38%)
- Appropriate antibiotic treatment, defined by an active drug administered within 24 h of infection, was administered to 41 (38%) patients: cefiderocol 20 (47%) and colistin 21 (32%)
- Clinical and microbiological outcomes by treatment are listed in **Table 6**

Table 6. Outcomes at Day 14 and Day 28[13]

Outcome	Cefiderocol (n=42)	Colistin (n=65)	*P* Value
Clinical cure (Day 14)	17 (40)	24 (36)	0.453
Microbiological cure (Day 14)	12 (28)	14 (21)	0.246
Death (Day 14)	17 (40)	33 (51)	0.147
Death (Day 28)	23 (55)	38 (58)	0.706

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

Narrative and Systematic Review of Published Case Series/Case Reports

Wicky et al (2023) reported the real-life experience of 16 patients treated with cefiderocol in the ICU for DTR non-fermenter infections at a single center in France between July 2020 and November 2021. Clinical cure was defined by improved clinical signs and oxygenation, decreased fever, and resolution of sepsis and organ dysfunction 2 days after EOT.[14]

Results[14]

- The most common non-fermenter infections were CRAB (62.5%), and *P. aeruginosa* (43.8%). The main source of infection was VABP in 14 (87.5%) patients
- Roughly half of the patients required supplemental organ support with 9 (56.3%) patients on ECMO, and 8 (50%) on RRT
- The clinical, microbiological, and safety outcomes of critically ill patients treated with cefiderocol are summarized in **Table 7**

Table 7. Clinical, Microbiological, and Safety Outcomes after Cefiderocol Treatment (N=16)[14]

Outcomes	All (N=16) n (%) or Median (IQR)
Antibiotic characteristics	
Duration of antibiotic course (days)	8 (7–13.5)
Antibiotic association[a]	5 (31.3)
Source control[b]	3 (18.8)
Clinical and microbiological outcomes	
Clinical failure	5 (31.3)
Persistent colonization	13 (81.3)
Relapse	9 (56.3)
Discharged from ICU	11 (68.8)
ICU length of stay (days)	60.5 (40–90.5)
ICU mortality	5 (31.3)
In-hospital death	6 (37.5)
1-year death	6 (37.5)
AEs	
C. difficile colitis	1 (6.3)
Hepatitis	3 (18.8)
Eosinophilia	1 (6.3)
Encephalopathy	9 (56.3)
Rash	1 (6.3)

Abbreviations: AE, adverse event; ICU, intensive care unit; IQR, interquartile range.
[a]At least 2 or 3 antibiotics (administered intravenously or nebulized).
[b]Surgery or catheter removal.
Table adapted from Wicky et al. *Antibiotics (Basel)*. 2023.

Narrative and Systematic Review of Published Case Series/Case Reports (Cont.)

Viale et al (2022) described the real-world experience of cefiderocol during the initial clinical phase of patients who received cefiderocol in the compassionate use or expanded access program.[15]

Methods[15]

- This systematic literature review included published case reports or case series that reported at least 1 of the following outcomes:
  - ACM
  - Clinical improvement
  - Microbiological eradication
  - Discharge status
  - AEs
- The literature search was finalized in December 2021. The following databases were searched: clinicaltrials.gov, Cochrane Database of Systematic Reviews, (CDSR) Cochrane Central Register of controlled trials (CENTRAL), the Database of Abstracts of Reviews of Effects (DARE) Embase, the HTA database, OVID MEDLINE, PubMed, and the WHO International Clinical Trial Registry Portal (ICTRP)

Results[15]

- Overall, 150 patients in 44 studies, including 41 case reports and 3 case series publications, were analyzed. The ages ranged from 2 to 84 years
- The most frequent type of infection was pneumonia/RTI in 22% of patients, while bacteremia was reported for 10.7% of patients. Overall, 27 (18%) patients had SARS-CoV-2 infection. Osteomyelitis and burns each diagnosed in 5.3%, surgical site infection in 4%, prosthetic joint infection in 1.3%, colonic perforation in 0.7% of patients, and other diagnoses in 24% of patients
- The 2 most frequent pathogens were *A. baumannii* (n=56, 37.3%) and *P. aeruginosa* (n=59, 59.3%). Also, *Achromobacter* spp. was identified in a total of 14 (9.3%) patients, *K. pneumoniae* in 7 (4.7%) patients, and *S. maltophilia* and *Enterobacter hormaechei* in 2 (1.3%) patients each
- Clinical outcomes were reported for 92 patients, of which cure was reported for 74 patients (80%) and failure was observed in 18 patients (20%). There was no report on clinical outcome for 58 patients. The number of patients with clinical improvement by pathogen is shown in **Table 8**
- Microbiological outcomes were reported for 78 patients, of which eradication was reported for 56 patients (72%) and failure was observed in 22 patients (28%). There was no report on microbiological outcome for 70 patients. The number of patients with microbiological eradication by pathogen is shown in **Table 9**
- The vital status was available for 123 patients. The ACM rate was 35% (43/123). There was no report of vital status for 27 patients. The vital status for patients by pathogen is shown in **Table 10**

Narrative and Systematic Review of Published Case Series/Case Reports (Cont.)

Table 8. Number of Patients with Clinical Cure by Pathogen[15]

Pathogen	Improvement	Failure	Not Reported
P. aeruginosa	19	3	28
A. baumannii	18 (5)	6 (2)	11 (13)
A. xylosoxidans	8	1	0
K. pneumoniae	4 (1)	0	1
Achromobacter	2	0	3
E. coli	2	0	1
E. hormaechei	1	0	0
E. cloacae	0	0	1
S. maltophilia	1	0	0
P. rettgeri	0	1	0
Multiple pathogens	3 (1)	0 (1)	0
Unclear pathogens	0 (9)	0 (4)	0
Overall total number of patients	**74**	**18**	**58**

Data were reported for 92 patients, no data were reported for 58 patients.
Clinical cure was defined by individual study authors, and as such varied across the included studies.
Numbers in parentheses report data from case series studies.
Table adapted from Viale et al. IDWeek. 2022.

Table 9. Number of Patients with Microbiological Eradication by Pathogen[15]

Pathogen	Improvement	Failure	Not Reported
P. aeruginosa	12	2	35 (9)
A. baumannii	19 (11)	2 (9)	14 (2)
A. xylosoxidans	1	8	0
K. pneumoniae	4 (1)	0	1 (1)
Achromobacter	1	0	4
E. coli	1	0	2
E. hormaechei	1	0	0 (1)
E. cloacae	0	1	0
S. maltophilia	1	0	0
P. rettgeri	0	0	0
Multiple pathogens	2 (2)	0	1
Overall total number of patients	**56**	**22**	**70**

Data were reported for 78 patients.
Data were not reported for 70 patients and 2 patients were found to have pathogens that were not susceptible to cefiderocol.
Numbers in parentheses report data from case series studies.
Table adapted from Viale et al. IDWeek. 2022.

Narrative and Systematic Review of Published Case Series/Case Reports (Cont.)

Table 10. ACM by Pathogen[15]

Pathogen	Alive	Dead	Not Reported
P. aeruginosa	27 (3)	13 (2)	10
A. baumannii	20 (17)	12 (8)	3
A. xylosoxidans	1	0	8
K. pneumoniae	2 (1)	2	1
Achromobacter	1	0	4
E. coli	3	0	0
E. hormaechei	0 (1)	0	1
E. cloacae	0	1	0
S. maltophilia	0	1	0
P. rettgeri	0	1	0
Multiple pathogens	3 (1)	0 (2)	0
Unclear pathogens	0	0 (1)	0
Overall total number of patients	**80**	**43**	**27**

Abbreviation: ACM, all-cause mortality.
Data were reported for 123 patients, no data were reported for 27 patients.
Numbers in parentheses report data from case series studies.
Table adapted from Viale et al. IDWeek. 2022.

- The most frequent type of infection was pneumonia/RTI in 22% of patients, while bacteremia was reported for 10.7% of patients. Overall, 27 (18%) patients had SARS-CoV-2 infection. Osteomyelitis and burns each diagnosed in 5.3%, surgical site infection in 4%, prosthetic joint infection in 1.3%, colonic perforation in 0.7% of patients, and other diagnoses in 24% of patients
- The 2 most frequent pathogens were *A. baumannii* (n=56, 37.3%) and *P. aeruginosa* (n=59, 59.3%). Also, *Achromobacter* spp. was identified in a total of 14 (9.3%) patients, *K. pneumoniae* in 7 (4.7%) patients, and *S. maltophilia* and *Enterobacter hormaechei* in 2 (1.3%) patients each
- Clinical outcomes were reported for 92 patients, of which cure was reported for 74 patients (80%) and failure was observed in 18 patients (20%). There was no report on clinical outcome for 58 patients. The number of patients with clinical improvement by pathogen is shown in **Table 8**
- Microbiological outcomes were reported for 78 patients, of which eradication was reported for 56 patients (72%) and failure was observed in 22 patients (28%). There was no report on microbiological outcome for 70 patients. The number of patients with microbiological eradication by pathogen is shown in **Table 9**
- The vital status was available for 123 patients. The ACM rate was 35% (43/123). There was no report of vital status for 27 patients. The vital status for patients by pathogen is shown in **Table 10**

Fetroja® – Real-World Evidence

This medical response contains information in addition to that provided in the Fetroja® (cefiderocol) for injection, for intravenous use Full Prescribing Information approved by the U.S. Food and Drug Administration (FDA). Shionogi does not recommend the use of Fetroja in any manner other than as described in the Full Prescribing Information. **Please read the attached Fetroja Full Prescribing Information**.

Relevant Prescribing Information

Fetroja® is indicated in patients 18 years of age or older for the treatment of:[16]

- 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:[16]

- 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**

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Literature Search

As of April 2025, a computerized search of the published medical literature using internal and external databases (ie, Medline® and Embase®) has identified several relevant references regarding the use of cefiderocol in the real-world setting. For your review, these references are listed in the bibliography as follows:

- Clancy CJ, Cornely OA, Marcella SW, Nguyen ST, Gozalo L, Cai B. Effectiveness and safety of cefiderocol in clinical practice for treatment of patients with Gram-negative bacterial infections: US interim results of the PROVE study. *Infect Drug Resist*. 2024;17:4427-4443. [Web Link]
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Literature Search (Cont.)

- Briceño Casado M, Criado-Rubio B, Gil-Sierra M, et al. Use of cefiderocol for multidrug-resistant *Acinetobacter baumannii* in patients with SARS-CoV-2: two case reports [5PSQ-030]. *Eur J Hosp Pharm*. 2022;29(Suppl 1):A127-A128. [Web Link]
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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	IPTW	inverse probability of treatment weighting
AE	adverse event	IQR	interquartile range
aHR	adjusted hazard ratio	IU	international units
aOR	adjusted odds ratio	IV	intravenous
BJI	bone and joint infection	LRTI	lower respiratory tract infection
BSI	bloodstream infection	MBL	metallo-β-lactamase
CCI	Charlson Comorbidity Index	MDR	multi-drug resistant
CI	confidence interval	MI	myocardial infarction
CKD	chronic kidney disease	MIC	minimum inhibitory concentration
COPD	chronic obstructive pulmonary disease	NDM	New Delhi metallo-β-lactamase
COVID-19	Coronavirus disease 19	q8h	every 8 hours
CR	carbapenem-resistant	q12h	every 12 hours
CRAB	carbapenem-resistant *A. baumannii*	QID	once a day
CR-BSI	catheter-related bloodstream infection	RRT	renal replacement therapy
cUTI	complicated urinary tract infection	RTI	respiratory tract infection
DTR	difficult-to-treat resistant	SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
ECMO	extracorporeal membrane oxygenation	SOFA	Sequential Organ Failure Assessment
EOT	end of treatment	SSTI	skin and soft tissue infection
FDA	US Food and Drug Administration	TID	three times a day
g	grams	US	United States
h	hours	UTI	urinary tract infection
HABP	hospital-acquired bacterial pneumonia	VABP	ventilator-associated bacterial pneumonia
HR	hazard ratio	VHA	Veterans Health Administration
HSCT	hematopoietic stem cell transplant	VIM	Verona integron-encoded MBL
IAI	intra-abdominal infection	WLS	withdrawal of life support

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Enclosure

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