Fetroja® – Activity against Resistant *Pseudomonas aeruginosa*

SHIONOGI

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Summary

CLINICAL STUDIES

- **APEKS-cUTI**, a Phase 2, multicenter, double-blind, parallel-group, non-inferiority trial evaluated the efficacy and safety of cefiderocol in patients hospitalized with cUTI with or without pyelonephritis or AUP, who were randomized to receive 1 h IV infusions of cefiderocol 2 g or imipenem–cilastatin 1 g q8h for 7–14 days[1]
  - In *Pseudomonas aeruginosa* isolates that were resistant to imipenem, cefepime, levofloxacin, or piperacillin–tazobactam, the eradication rates ranged from 33.3–66.7% in patients treated with cefiderocol[2]
- **APEKS-NP**, a Phase 3, multicenter, randomized, double-blind, non-inferiority trial, assessed the efficacy and safety of cefiderocol in patients with HABP, VABP or HCABP caused by suspected Gram-negative pathogens, who were randomized to receive 3 h IV infusions of either cefiderocol 2 g or meropenem 2 g q8h for 7–14 days, in addition to adjunctive linezolid (600 mg q12h for at least 5 days)[3,4]
  - The Day 14 ACM in patients with *P. aeruginosa* was 8% (2/24) in the cefiderocol arm compared to 13% (3/23) in the meropenem arm (treatment difference [95% CI]: –4.7 [–22.4 to 12.9])[3]
  - The Day 28 ACM in patients with *P. aeruginosa* was 8% (2/24) in the cefiderocol arm compared to 26% (6/23) in the meropenem arm (treatment difference [95% CI]: –17.8 [–38.8 to 3.3])[4]
  - The ACM rate at Day 14 was 0% for *P. aeruginosa* isolates with meropenem MICs>8 µg/mL in both the cefiderocol group and the meropenem group[5]
- **CREDIBLE-CR**, a randomized, open-label, multicenter, descriptive Phase 3 trial assessed the efficacy and safety of cefiderocol compared to BAT in patients with HABP, VABP, HCABP, BSI, sepsis, or cUTI caused by CR Gram-negative pathogens, with no hypothesis testing or formal inferential analyses. Cefiderocol 2 g q8h over a 3 h IV infusion or IV BAT was administered for 7–14 days[6]
  - The ACM was higher in the cefiderocol group, 6/17 (35%), than the BAT group, 2/12 (17%), for patients with polymicrobial *P. aeruginosa* and *Acinetobacter* spp. infections, but was identical in patients with only *P. aeruginosa* infections, 2/11 (18%), for both treatment arms[6]

REAL-WORLD EVIDENCE

- **Torre-Cisneros et al (2025)** reported the results from the PERSEUS study, which was a retrospective, multicenter, medical chart review study in hospitalized patients (N=261) with Gram-negative bacterial infections in Spain. 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)[7]
  - In the *P. aeruginosa* subgroup, cefiderocol was used as first-line treatment in 25 (14.4%) patients, the median treatment duration of cefiderocol treatment was 11 days, and cefiderocol was used in combination with other antibiotics in 56 (32.9%) patients
  - In the *P. aeruginosa* subset (n=174), clinical cure was achieved in 147 (84.5%) patients and Day 28 ACM occurred in 30 (17.2%) patients

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Summary (Cont.)

REAL-WORLD EVIDENCE (Cont.)

- **Clancy et al (2024)** described the US PROVE interim analysis where 53/82 (64.6%) patients treated with cefiderocol for monomicrobial *P. aeruginosa* achieved clinical cure. In polymicrobial *P. aeruginosa* infections, the clinical cure rates ranged from 42.9–75% with various concomitant pathogens including *Acinetobacter baumannii*, Enterobacterales, and *Stenotrophomonas maltophilia*[8]

- **Clancy et al (2024)** reported the final results of the PROVE study that included patients from the US and Europe. For patients with infections due to *P. aeruginosa*, the clinical cure and clinical response rate was 72% and 79.3%, respectively. The ACM at Day 30 was 19.9% for patients with *P. aeruginosa* infection[9]

- **Chou et al (2023)** performed a prospective, real-world observational study evaluating clinical and microbiological outcomes in patients receiving cefiderocol within the VHA system[10]
  - Among patients with monomicrobial *P. aeruginosa* infections, clinical failure occurred in 33.3% of patients and the 30-day and 90-day ACM rates were 22.2% and 44.4%, respectively. Microbiologic failure at 30 and 90 days occurred in 33.3% and 44.4% of patients

- **Satlin et al (2022)** evaluated patients (N=46) with *P. aeruginosa* infections from the compassionate use program who were treated with cefiderocol[11]
  - Clinical response was achieved by 33 (72%) patients, and the Day 28 ACM was 24%
  - Cefiderocol was active against 91% of the 46 isolates studied (CLSI 2022 breakpoint), and the cefiderocol $MIC_{50/90}$ was 0.5 µg/mL and 4 µg/mL, respectively

SURVEILLANCE STUDIES

- **Kimbrough et al (2025)** evaluated the activity of cefiderocol and various BL–BLI combinations against various subsets of *P. aeruginosa* isolates (n=9572) collected from hospitalized patients in 36 US and 43 primarily European hospitals as part of the SENTRY Antimicrobial Surveillance Program between 2020 and 2023[12]
  - A DTR phenotype was identified in 377 isolates, and cefiderocol retained activity in 88.9–98.1% of cases (by contrast, the 3 BL–BLI combinations tested demonstrated lower activity, with a susceptibility range of 52.3–56%)
  - Cefiderocol retained activity against both non-carbapenemase and carbapenemase-carrying isolates with a susceptibility range of 82.6–100%, while the 3 tested BL–BLI combinations were almost completely inactive against the carbapenemase-carrying subsets and showed limited activity against the non-carbapenemase group (susceptibility ranging from 63.7–69.6%)

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Summary (Cont.)

SURVEILLANCE STUDIES (Cont.)

- **Mendes et al (2025)** examined the *in vitro* activity of cefiderocol and comparator agents against *P. aeruginosa* isolates (including resistant subsets), collected from US hospitals during the SENTRY Antimicrobial Surveillance Program (2020–2024)[13]
  - MDR *P. aeruginosa* isolates were demonstrated to be 95.5–99.1% susceptible to cefiderocol, while DTR and XDR isolates were 91.6–98.4% and 88.8–96.6% susceptible, respectively
  - Of the agents tested, cefiderocol had the lowest MIC (96.8–99.4% susceptible) against Carb-NS *P. aeruginosa* (a MIC_{90} ≥4-fold lower than all comparator agents)
- **Yamano et al (2025)** tracked the *in vitro* activity of cefiderocol over a 5-year period against Gram-negative bacterial isolates collected from hospitalized patients across the US and Europe during the SENTRY Antimicrobial Surveillance Program between 2020 and 2024[14]
  - Consistently high activity was observed for cefiderocol against Enterobacterales, *P. aeruginosa*, *A. baumannii* complex and *S. maltophilia* over the 5-year period
  - %S for all *P. aeruginosa* isolates was 98.8–100% (95.3–100% for the Carb-NS subsets)
- **DeJonge et al (2025)** assessed the potential degree of cross resistance to cefiderocol and various BL–BLI combinations in Gram-negative bacterial isolates collected from hospitalized patients across the US and Europe during the SENTRY Antimicrobial Surveillance Program between 2020 and 2024[15]
  - Overall, 4.2%, 4.1%, and 3.5% of *P. aeruginosa* isolates were determined to be NS to ceftolozane–tazobactam, ceftazidime–avibactam, and imipenem–relebactam, respectively, although these percentages appear to show an upward trend over the study period
  - Cefiderocol retained activity against *P. aeruginosa* isolates NS to various BL–BLI combinations
- **Mendes et al (2024)** examined the *in vitro* activity of cefiderocol and comparator agents against *P. aeruginosa* isolates carrying MBL genes that had been collected in the US and Europe between 2020–2023 as part of the SENTRY Antimicrobial Surveillance Program[16]
  - Against the overall population of Carb-NS *P. aeruginosa* isolates, cefiderocol had a MIC_{50} of 0.12 mg/L and a MIC_{90} of 0.5 mg/L (96–99.4% susceptible)
  - Cefiderocol (85–96% susceptible) demonstrated activity against the MBL-carrying *P. aeruginosa* subset of isolates with a MIC_{50} value of 0.25 mg/L and a MIC_{90} of 2 mg/L

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Summary (Cont.)

SURVEILLANCE STUDIES (Cont.)

- **DeJonge et al (2023)** evaluated the activity of cefiderocol and comparator antibiotics against 299 DTR *P. aeruginosa* isolates collected from hospitalized patients in the US and Europe (2020–2022)[17]
  - Cefiderocol was the most active against DTR *P. aeruginosa* with susceptibility rates of 98.3% per CLSI and 89.6% per FDA breakpoints
- **Shields et al (2023)** evaluated the *in vitro* activity of cefiderocol against 178 *P. aeruginosa* isolates at baseline and post-exposure to ceftolozane–tazobactam, ceftazidime–avibactam, and imipenem–relebactam[18]
  - Cefiderocol MICs were <2 mg/L in 94% of isolates, with a MIC_{50} and MIC_{90} of 0.06 mg/L and 0.25 mg/L, respectively
  - The median MIC for cefiderocol doubled from 0.12 mg/L to 0.25 mg/L against isolates that were collected following exposure to any of these BL–BLIs (n=47) compared to baseline isolates that were from the same patients (n=31; *P*=0.1442)

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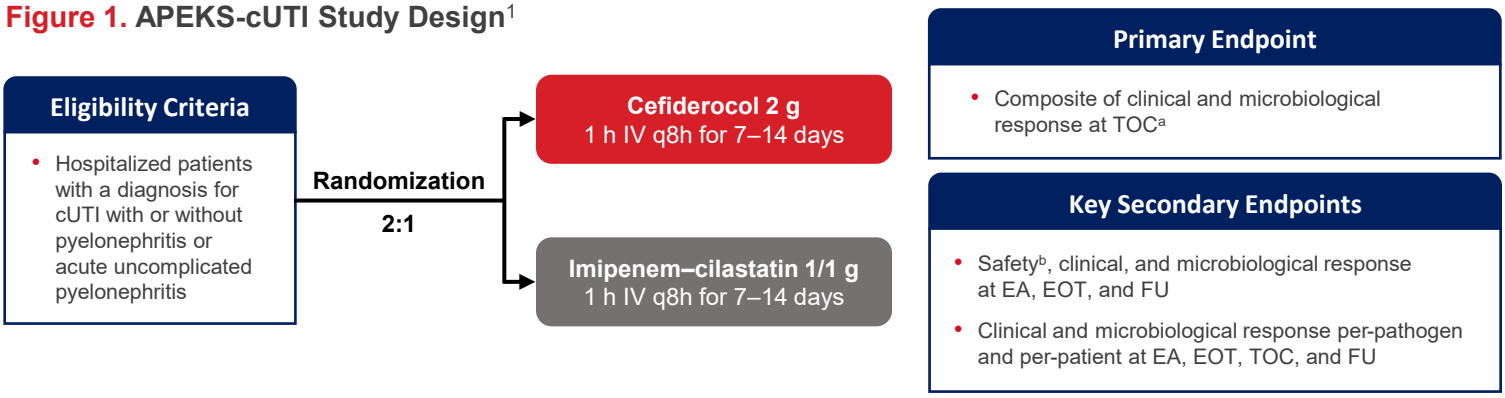
Clinical Studies

APEKS-cUTI

Methods

- APEKS-cUTI (NCT02321800) was a Phase 2, multicenter, randomized, double-blind, parallel-group, non-inferiority study that assessed the efficacy and safety of cefiderocol in cUTI caused by suspected Gram-negative pathogens[1]
- The non-inferiority margin was 15%[1]

Figure 1. APEKS-cUTI Study Design[1]



Abbreviations: CFU, colony-forming unit; cUTI, complicated urinary tract infection; EA, early assessment; EOT, end of treatment; FU, follow-up; g, grams; h, hours; IV, intravenous; mITT, modified intention-to-treat; q8h, every 8 hours; TOC, test of cure.
[a]In the mITT population defined as all randomly assigned individuals who received ≥1 dose of study drug and had qualifying Gram-negative uropathogen (≥1x10^5 CFU/mL).
[b]Safety assessed in all randomly assigned individuals who received ≥1 dose of study drug, according to the treatment they received.

Results

- A total of 371 patients were included in the mITT population (n=252 cefiderocol; n=119 imipenem–cilastatin) received treatment[1]
- In the mITT population, 18 (7.1%) patients treated with cefiderocol had *P. aeruginosa* isolated at baseline[2]
- These isolates were resistant to imipenem, cefepime, levofloxacin, or piperacillin–tazobactam. Microbiological eradication rates for drug-resistant *P. aeruginosa* are shown in Table 1

Table 1. Microbiological Eradication Rate per Select Resistant Pathogen at Baseline in the m-ITT Population[2]

Pathogen Resistant to Antibiotic	Cefiderocol		Imipenem–Cilastatin	
	N	Eradication, n (%)	N	Eradication, n (%)
P. aeruginosa				
Imipenem	3		1	0
Cefepime	2		0	NA
Levofloxacin	10	6 (60)	3	1 (33.3)
Piperacillin–tazobactam	3	1 (33.3)	0	NA

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Table 1. Microbiological Eradication Rate per Select Resistant Pathogen at Baseline in the m-ITT Population[2]

Pathogen Resistant to Antibiotic	Cefiderocol		Imipenem–Cilastatin	
	N	Eradication, n (%)	N	Eradication, n (%)
P. aeruginosa				
Imipenem	3	2 (66.7)	1	0
Cefepime	2	1 (50)	0	NA
Levofloxacin	10	6 (60)	3	1 (33.3)
Piperacillin–tazobactam	3	1 (33.3)	0	NA

Abbreviations: mITT, modified intention-to-treat; NA, not available.
Table adapted from Portsmouth et al. *Lancet Infect Dis*. 2018.

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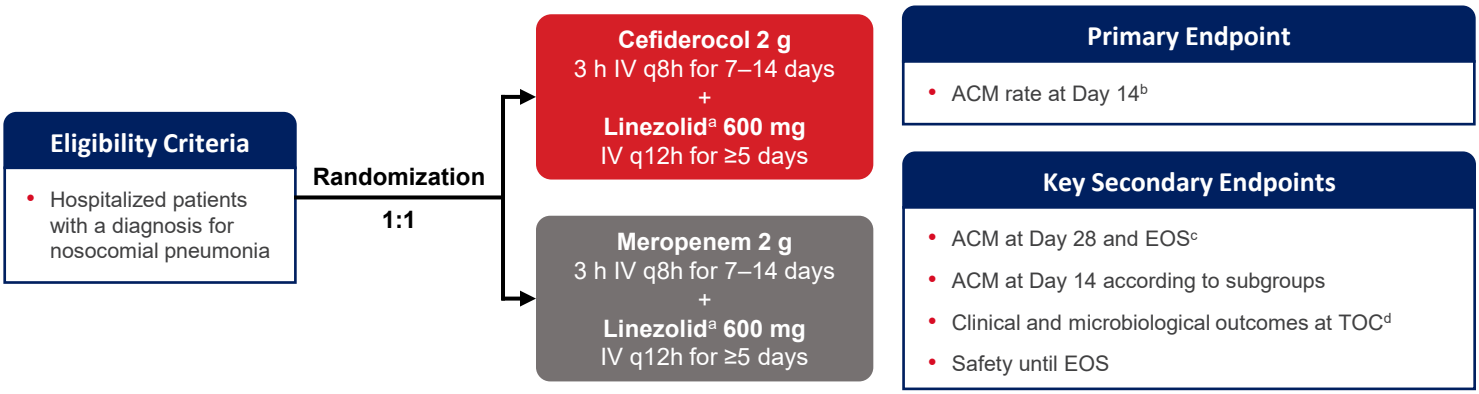
Clinical Studies (Cont.)

APEKS-NP

Methods

- APEKS-NP (NCT03032380) was a Phase 3, multicenter, randomized, double-blind, parallel-group, non-inferiority study that assessed the efficacy and safety of cefiderocol in VABP, HABP, or HCABP caused by suspected Gram-negative pathogens[3]

Figure 2. APEKS-NP Study Design[3]



Abbreviations: ACM, all-cause mortality; EOS, end of study; EOT, end of treatment; g, grams; h, hours; IV, intravenous; LRTI, lower respiratory tract infection; mITT, modified intention-to-treat; q8h, every 8 hours; q12h, every 12 hours; TOC, test of cure.
[a]Administered to cover Gram-positive bacteria.
[b]In the mITT population (noninferiority margin, -12.5%), defined as all randomized patients who received ≥1 dose of a study drug and had evidence of a Gram-negative LRTI.
[c]EOT + 28 days (±3 days).
[d]EOT + 7 days (±2 days).

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Clinical Studies (Cont.)

APEKS-NP (Cont.)

Results

- The mITT population comprised 292 patients (n=145 cefiderocol; n=147 meropenem)[3]
- A total of 24 (17%) patients in the cefiderocol group and 24 (16%) patients in the meropenem group were diagnosed with a Gram-negative infection caused by *P. aeruginosa*[3]
- The Day 14 ACM in patients with *P. aeruginosa* was 2 (8%) in the cefiderocol arm compared to 3 (13%) in the meropenem arm (treatment difference, [95% CI]: –4.7 [–22.4; 12.9])[3]
  - The Day 28 ACM in patients with *P. aeruginosa* was 2 (8%) in the cefiderocol arm compared to 6 (26%) in the meropenem arm (treatment difference, [95% CI]: –17.8 [–38.8; 3.3])[4]
- The Day 14 ACM was 0% for *P. aeruginosa* isolates with meropenem MICs >8 µg/mL in both the cefiderocol group and the meropenem group[5]
- ACM for *P. aeruginosa* at Day 28 and at EOS based on meropenem MICs are shown in Table 2 and Table 3

Table 2. ACM at Day 28 for *P. aeruginosa* Isolates with Meropenem MIC>8 µg/mL (mITT Population)[5]

	Cefiderocol (N=145)	Meropenem (N=147)
Meropenem MIC>8 µg/mL		1/6 (16.7)
Meropenem MIC>16 µg/mL		1/4 (25)
Meropenem MIC>32 µg/mL		1/3 (33.3)
Meropenem MIC>64 µg/mL		1/2 (50)

Table 3. ACM at EOS for *P. aeruginosa* Isolates with Meropenem MIC>8 µg/mL (mITT Population)[5]

	Cefiderocol (N=145)	Meropenem (N=147)
Meropenem MIC>8 µg/mL		1/6 (16.7)
Meropenem MIC>16 µg/mL		1/4 (25)
Meropenem MIC>32 µg/mL		1/3 (33.3)
Meropenem MIC>64 µg/mL		1/2 (50)

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Clinical Studies (Cont.)

Table 2. ACM at Day 28 for *P. aeruginosa* Isolates with Meropenem MIC>8 µg/mL (mITT Population)[5]

	Cefiderocol (N=145)	Meropenem (N=147)
Meropenem MIC>8 µg/mL	0/6 (0)	1/6 (16.7)
Meropenem MIC>16 µg/mL	0/6 (0)	1/4 (25)
Meropenem MIC>32 µg/mL	0/5 (0)	1/3 (33.3)
Meropenem MIC>64 µg/mL	0/1 (0)	1/2 (50)

Data expressed as n/N (%).
Abbreviations: MIC, minimum inhibitory concentration; mITT, modified intent-to-treat.

Table 3. ACM at EOS for *P. aeruginosa* Isolates with Meropenem MIC>8 µg/mL (mITT Population)[5]

	Cefiderocol (N=145)	Meropenem (N=147)
Meropenem MIC>8 µg/mL	1/6 (16.7)	1/6 (16.7)
Meropenem MIC>16 µg/mL	1/6 (16.7)	1/4 (25)
Meropenem MIC>32 µg/mL	1/5 (20)	1/3 (33.3)
Meropenem MIC>64 µg/mL	0/1 (0)	1/2 (50)

Data expressed as n/N (%).
Abbreviations: EOS, end of study; MIC, minimum inhibitory concentration; mITT, modified intent-to-treat.

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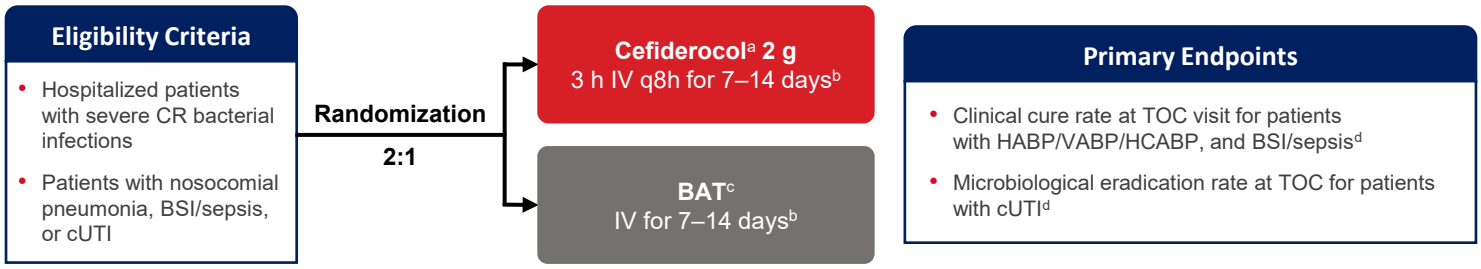
Clinical Studies (Cont.)

CREDIBLE-CR

Methods

- CREDIBLE-CR (NCT02714595) was a Phase 3, prospective, open-label, multicenter, randomized, parallel-group, descriptive study that assessed the efficacy and safety of cefiderocol and BAT in hospitalized patients with severe CR bacterial infections[6]
- CREDIBLE-CR was a descriptive study with no hypothesis testing or formal inferential analyses[6]

Figure 3. CREDIBLE-CR Study Design[6]



Abbreviations: BAT, best available therapy; BSI, bloodstream infection; CR, carbapenem-resistant; cUTI, complicated urinary tract infection; g, grams; h, hours; HABP, hospital-acquired bacterial pneumonia; HCABP, healthcare-associated bacterial pneumonia; IV, intravenous; q8h, every 8 hours; TOC, test of cure; VABP, ventilator-associated bacterial pneumonia.
[a]Could be complemented with 1 adjunctive antibiotic therapy, excluding polymyxins, cephalosporins, and carbapenems and combinations with a β-lactamase inhibitor.
[b]Could be extended up to 21 days at the discretion of the investigator.
[c]Selected before randomization and could consist of up to 3 systemic antibiotics.
[d]Evaluated in the CR-Micro-ITT population, defined as all patients with a confirmed CR Gram-negative pathogen who received ≥1 dose of study drug.

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Clinical Studies (Cont.)

CREDIBLE-CR (Cont.)

Results

- A total of 152 patients were randomly assigned to cefiderocol or BAT, of whom 150 patients (n=101 cefiderocol; n=49 BAT) received treatment (ITT and safety population)[6]
- A total of 118 patients were included in the CR-Micro-ITT population, which included patients randomized to cefiderocol (n=80) and BAT (n=38) whose baseline Gram-negative pathogen was CR as confirmed by central laboratory testing[6]
- Within the CR-Micro-ITT population, there were 12 (15%) patients in the cefiderocol arm and 10 (26%) patients in the BAT arm with *P. aeruginosa*
- The clinical cure and microbiological eradication rates in patients with *P. aeruginosa* infections are shown in **Table 4**
- Outcomes for patients with MDR *P. aeruginosa* isolates have not been evaluated in CREDIBLE-CR[19]

Table 4. Clinical and Microbiological Outcomes at TOC in Patients with *P. aeruginosa* Infections (CR-Micro-ITT Population)[20]

Outcome	Cefiderocol (N=12)	BAT (N=10)
Clinical Outcomes, n (%)		
Clinical cure		5 (50)
Clinical failure		4 (40)
Indeterminate		1 (10)
Microbiological Outcomes, n (%)		
Eradication		2 (20)
Persistence	4 (33)	2 (20)
Indeterminate	7 (58)	6 (60)

Molecular Characterization

- Among 17 *P. aeruginosa* isolates in the cefiderocol group:[21]
  - 4 isolates expressed MBLs: VIM, IMP
  - 13 isolates did not possess carbapenemase genes
  - 10 isolates were porin channel OprD-deficient
  - The clinical and microbiological outcomes at the TOC for the cefiderocol and BAT group based on molecular characterization are shown in **Table 5**

Table 5. Clinical Cure Rates of Molecularly Characterized *P. aeruginosa* at TOC in the CR-Micro-ITT Population[21,22]

Molecular Characterization	Clinical Cure[b] n/N (%)	
	[illegible]col	BAT
MBL (VIM and IMP)-producing *P. aeruginosa*	[illegible]0)	2/3 (66.7)
OprD-deficient *P. aeruginosa*	7/10 (70)	5/10 (50)

Mortality[6]

- The overall ACM rate was 34/101 (34%) in the cefiderocol group and 9/49 (18%) in the BAT group through the EOS
- The ACM was higher in the cefiderocol group, 6/17 (35%), than the BAT group, 2/12 (17%), for patients with polymicrobial *P. aeruginosa* and *Acinetobacter* spp. infections but was identical in patients with only *P. aeruginosa* infections, 2/11 (18%) for both treatment arms

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Clinical Studies (Cont.)

Table 4. Clinical and Microbiological Outcomes at TOC in Patients with *P. aeruginosa* Infections (CR-Micro-ITT Population)[20]

Outcome	Cefiderocol (N=12)	BAT (N=10)
Clinical Outcomes, n (%)		
Clinical cure	7 (58)	5 (50)
Clinical failure	3 (25)	4 (40)
Indeterminate	2 (17)	1 (10)
Microbiological Outcomes, n (%)		
Eradication	1 (8)	2 (20)
Persistence	4 (33)	2 (20)
Indeterminate	7 (58)	6 (60)

Abbreviations: BAT, best-available therapy; CR-Micro-ITT, carbapenem-resistant microbiological intent-to-treat; TOC, test of cure.
Table adapted from Bassetti et al. *Lancet Infect Dis*. 2021 (Supplementary Appendix).

Table 5. Clinical Cure Rates of Molecularly Characterized *P. aeruginosa* at TOC in the CR-Micro-ITT Population[21,22]

Molecular Characterization	Clinical Cure[b] n/N (%)	
	Cefiderocol	BAT
MBL (VIM and IMP)-producing *P. aeruginosa*	4/4 (100)	2/3 (66.7)
OprD-deficient *P. aeruginosa*	7/10 (70)	5/10 (50)

Abbreviations: BAT, best available therapy; CR-Micro-ITT, carbapenem-resistant microbiological intent-to-treat; IMP, imipenemase; MBL, metallo-ß-lactamase; TOC, test of cure; VIM, Verona integron-encoded metallo-β-lactamase.
Table adapted from Matsunaga et al. IDWeek. 2020 and Timsit et al. *Clin Infect Dis*. 2022.

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Real-World Evidence

Torre-Cisneros et al (2025) reported the results from the PERSEUS study, which was a retrospective, multicenter, medical chart review study in hospitalized patients (N=261) with Gram-negative bacterial infections, excluding *Acinetobacter* spp., in Spain.[7]

Methods[7]

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 from treatment initiation 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
  - Clinical success was the composite outcome of clinical cure or survival at Day 28

Results[7]

- The most common Gram-negative pathogen was *P. aeruginosa*, isolated in 174 (66.7%) patients – additional pathogens included *Pseudomonas* spp. (n=15), *K. pneumoniae* (n=26), and other Enterobacterales (n=12)
- The most common infection sites caused by *P. aeruginosa* infections were respiratory (46.6%), urinary (16.1%), intra-abdominal (13.2%), and skin/soft tissue (12.6%)
- In the *P. aeruginosa* group, cefiderocol was used as first-line treatment in 25 (14.4%) patients, the median treatment duration of cefiderocol treatment was 11 days, and cefiderocol was used in combination with other antibiotics in 56 (32.9%) patients

Outcomes

- Overall, 210 (80.5%) patients achieved clinical cure at the end of treatment and ACM at Day 28 occurred in 56 (21.5%) patients
- In the *P. aeruginosa* subset (n=174), clinical cure was achieved in 147 (84.5%) patients and Day 28 ACM occurred in 30 (17.2%) patients
- Clinical cure and Day 28 ACM by infection site in the overall population and in the *P. aeruginosa* subset can be seen in Table 6

Table 6. Clinical Cure and Day-28 ACM by Infection Site in the Overall and *P. aeruginosa* Groups[7]

Infection Site	*P. aeruginosa* (N=174)		Overall (N=261)	
	Clinical Cure n/N (%)	Day-28 ACM n/N (%)	Clinical Cure n/N (%)	Day-28 ACM n/N (%)
Respiratory tract	64/81 (79)		95/125 (76)	34/125 (27.2)
Urinary tract	27/28 (96.4)		36/38 (94.7)	6/38 (15.8)
Intra-abdominal	16/23 (69.6)		26/38 (68.4)	9/38 (23.7)
Skin and skin structure	20/22 (90.9)		24/26 (92.3)	2/26 (7.7)
Bloodstream[a]	11/11 (100)		19/24 (79.2)	5/24 (20.8)
Bone and joint	6/6 (100)	0/6 (0)	6/6 (100)	0/6 (0)
Other	3/3 (100)[b]	0/3 (0)[b]	4/4 (100)[c]	0/4 (0)[c]

Safety

- In the screened population (N=314), 7 (2.2%) patients experienced an ADR
- 3 (1%) patients discontinued cefiderocol treatment due to an ADR and a serious ADR, and 1 death occurred due to a serious ADR (fatal toxic epidermal necrolysis)

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Table 6. Clinical Cure and Day-28 ACM by Infection Site in the Overall and *P. aeruginosa* Groups[7]

Infection Site	*P. aeruginosa* (N=174)		Overall (N=261)	
	Clinical Cure n/N (%)	Day-28 ACM n/N (%)	Clinical Cure n/N (%)	Day-28 ACM n/N (%)
Respiratory tract	64/81 (79)	18/81 (22.2)	95/125 (76)	34/125 (27.2)
Urinary tract	27/28 (96.4)	4/28 (14.3)	36/38 (94.7)	6/38 (15.8)
Intra-abdominal	16/23 (69.6)	5/23 (21.7)	26/38 (68.4)	9/38 (23.7)
Skin and skin structure	20/22 (90.9)	2/22 (9.1)	24/26 (92.3)	2/26 (7.7)
Bloodstream[a]	11/11 (100)	1/11 (9.1)	19/24 (79.2)	5/24 (20.8)
Bone and joint	6/6 (100)	0/6 (0)	6/6 (100)	0/6 (0)
Other	3/3 (100)[b]	0/3 (0)[b]	4/4 (100)[c]	0/4 (0)[c]

Abbreviations: ACM, all-cause mortality; BSI, bloodstream infection; CNS, central nervous system.
[a]Data are BSI of unknown origin/catheter-related BSI.
[b]Includes CNS infection (n=2) and mediastinitis (n=1).
[c]Includes CNS infection (n=2) and mediastinitis (n=2).
Table adapted from Torre-Cisneros et al. *Eur J Clin Microbiol Infect Dis*. 2025.

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Real-World Evidence (Cont.)

Clancy et al (2024) evaluated interim data between November 2020 and December 2023 (US subset analysis) from the PROVE study, a multicenter, retrospective, chart review study in patients treated with cefiderocol in European and US hospitals. Patients were eligible if they had a documented Gram-negative infection, including *P. aeruginosa*, along with the first-time use of cefiderocol for ≥72 h. Clinical cure was defined by resolution or improvement in infection signs and symptoms, without evidence of a later relapse and/or reinfection. ACM at Day 14 and 30 were also analyzed.[8]

Results[8]

- Of the 244 patients in the interim analysis, 82 (33.6%) had monomicrobial *P. aeruginosa* and 35 (14.3%) had polymicrobial *P. aeruginosa* with Enterobacterales (n=20), *S. maltophilia* (n=8), and *A. baumannii* (n=7) co-infections
- The most frequently observed sites for monomicrobial *P. aeruginosa* infections were respiratory (n=56), bloodstream (n=12), and skin and skin structure (n=6) infections
- The clinical cure rates for monomicrobial *P. aeruginosa* was 64.6% and ranged from 42.9–75% in polymicrobial infections – see **Table 7** for the clinical outcomes data

Table 7. Clinical Outcomes in Patients with *P. aeruginosa* Infections from the PROVE US Interim Analysis[8]

	n	Clinical Cure[a] n (%)	Clinical Response at EOT[b] n (%)	14-day IH-ACM n (%)	30-day IH-ACM n (%)
Monomicrobial infections by pathogen					
P. aeruginosa	82	53 (64	61 (74.4)	11 (13.4)	21 (25.6)
Polymicrobial infections by pathogen					
P. aeruginosa + *A. baumannii*	7	3 (42	4 (57.1)	2 (28.6)	2 (28.6)
P. aeruginosa + Enterobacterales	20	13 (65)	15 (75)	0 (0)	2 (10)
P. aeruginosa + *S. maltophilia*	8	6 (75)	7 (87.5)	0 (0)	0 (0)

Clancy et al (2024) reported the final results of the PROVE study for patients from the US and Europe. The outcomes for patients with infections caused by *P. aeruginosa* and treated with cefiderocol are described below:[9]

Results[9]

- Overall, *P. aeruginosa* was the most common species in monomicrobial infections (n=386)
- The clinical cure and clinical response rate for patients with infections due to *P. aeruginosa* was 72% and 79.3%, respectively
- The ACM at Day 30 was 19.9% for patients with *P. aeruginosa* infection

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Real-World Evidence (Cont.)

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	n	Clinical Cure[a] n (%)	Clinical Response at EOT[b] n (%)	14-day IH-ACM n (%)	30-day IH-ACM n (%)
Monomicrobial infections by pathogen					
P. aeruginosa	82	53 (64.6)	61 (74.4)	11 (13.4)	21 (25.6)
Polymicrobial infections by pathogen					
P. aeruginosa + *A. baumannii*	7	3 (42.9)	4 (57.1)	2 (28.6)	2 (28.6)
P. aeruginosa + Enterobacterales	20	13 (65)	15 (75)	0 (0)	2 (10)
P. aeruginosa + *S. maltophilia*	8	6 (75)	7 (87.5)	0 (0)	0 (0)

Abbreviations: ACM, all-cause mortality; EOT, end of treatment; IH, in-hospital; US, United States.
[a]Clinical cure: resolution or improvement of signs and symptoms without a later relapse, excluding patients who had a relapse or reinfection after EOT.
[b]Clinical response: resolution or improvement of signs and symptoms at EOT.
Table adapted from Clancy et al. *Infect Drug Resist*. 2024.

- **Clancy et al (2024)** reported the final results of the PROVE study for patients from the US and Europe. The outcomes for patients with infections caused by *P. aeruginosa* and treated with cefiderocol are described below.[10]

Results[10]

- Overall, *P. aeruginosa* was the most common species in monomicrobial infections (n=386)
- The clinical cure and clinical response rate for patients with infections due to *P. aeruginosa* was 72% and 79.3%, respectively
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Real-World Evidence (Cont.)

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 and received at least 2 days of cefiderocol treatment.[10]

- 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[10]

- 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%)
- Among patients with monomicrobial *P. aeruginosa* infections, clinical failure occurred in 6 (33.3%) patients and the 30-day and 90-day ACM rates were 22.2% and 44.4%, respectively
- Microbiologic failure at 30 and 90 days occurred in 6 (33.3%) and 8 (44.4%) patients, respectively

Table 8. Antimicrobial Susceptibility Testing and Molecular Characterization Results for *P. aeruginosa* (N=39)[10]

Agent(s)	n/N (%)
Cefiderocol	15/17 (88.2)
Ceftolozane–tazobactam	11/24 (45.8)
Imipenem–relebactam	1/6 (16.7)
Ceftazidime–avibactam	4/16 (25)
Polymyxins	1/7 (14.3)
Carbapenems	5/37 (13.5)
Cefepime	5/34 (14.7)
Ceftazidime	9/29 (31)
Piperacillin–tazobactam	12/32 (37.5)
Aminoglycosides	31/38 (81.6)
Fluoroquinolones	7/39 (17.9)
Molecular tests	VIM, 1 ND, 7

ND, carbapenemase genes not detected by molecular testing. Patients may have ≥1 strains of an organism. For example, a patient with 2 different strains of *P. aeruginosa*, each strain will be included above.
Abbreviations: ND, not detected; VIM, Verona integron-encoded metallo-β-lactamase.
Table adapted from Chou et al. *Antimicrob Steward Healthc Epidemiol*. 2023.

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Real-World Evidence (Cont.)

Satlin et al (2023) performed an analysis of a subset of 46 patients treated with cefiderocol for MDR or CR *P. aeruginosa* as part of the compassionate use program. The β-lactamase content, *in vitro* activity of the isolates, and clinical outcomes (eg Day 28 ACM and clinical response) by MIC values were evaluated.[11]

Methods[11]

- Patients from the US, Europe, or Canada that received cefiderocol (2016–2020) were included
- Only descriptive statistics were reported
- Clinical response was described by the treating physician as 'cure and discharge', 'improvement', 'response', 'stabilization', or 'no response' and a prespecified definition was not provided by the manufacturer

Results[11]

Infection/isolate characteristics

- The most common infection types were respiratory tract (50%), bloodstream (33%), and wound (22%) infections
- The most common comorbidities were respiratory/pulmonary disease (48%), acute or chronic kidney diseases (43%), and cardiovascular disorder (26%)
- The cefiderocol MIC_{50} and MIC_{90} was 0.5 µg/mL and 4 µg/mL, respectively
  - Overall, 91% of *P. aeruginosa* isolates were susceptible according to the CLSI breakpoint (≤4 µg/mL) and 63% were susceptible based on FDA breakpoints (≤1 µg/mL)
  - Of the 46 isolates, 44 were MDR
- Of isolates with molecular characterization, Class A (GES, VEB, and PER) and B (NDM, VIM, and IMP) β-lactamases were found in 20% of isolates each. All isolates contained class C PDC genes
  - The cefiderocol MIC was ≤4 µg/mL for all isolates that produced Class B β-lactamases

Cefiderocol utilization

- The median (range) cefiderocol duration was 22.5 days (1–132)
- The most common concomitant antibiotics included polymyxins (48%), aminoglycosides (24%), carbapenems (22%), newer BL–BLIs (20%), and eravacycline (7%)

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Real-World Evidence (Cont.)

Results (Cont.)[11]

Outcomes

- Clinical response was achieved by 33 (72%) patients. Clinical response was not reported or unknown in 7 (15%) patients
  - No correlation was seen between clinical response and cefiderocol MIC values – see **Table 9**
  - Of the patients with MBL-positive *P. aeruginosa*, 6 of 9 (67%) achieved a clinical response and the response was unknown for the other 3 patients (33%)
- Of the patients (n=42) with recorded vital status at Day 28, 10 (24%) patients died – see **Table 9**
  - No deaths were considered to be related to cefiderocol

Table 9. Outcomes Based on Cefiderocol MIC[11]

	S based on FDA breakpoints (MIC≤1 µg/mL)	S based on CLSI, NS by FDA breakpoints (MIC=2–4 µg/mL)	NS by FDA and CLSI breakpoints (MIC=8–16 µg/mL)
Clinical response	N=29	N=13	N=4
Yes	20 (69)	9 (69)	4 (100)
No	4 (14)	2 (15)	
Not reported	5 (17)	2 (15)	
Known vital status	N=26	N=12	N=not provided
Day 28 mortality	6 (23.1)	4 (33.3%)	0 (0%)

Safety

- AEs were reported in 19 (41%) patients
  - The AEs were related or possibly related to cefiderocol for 3 patients (n=1 each)
    - Increased liver enzymes (confounded by liver transplant and hepatic abscesses following surgery) which resolved following cefiderocol discontinuation
    - Thrombocytopenia, which resolved after cefiderocol treatment was completed, as well as *Clostridioides difficile* infection
    - Acute interstitial nephritis (confounded by obstructive uropathy and chronic kidney disease) which resolved following cefiderocol discontinuation

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Real-World Evidence (Cont.)

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	S based on FDA breakpoints (MIC≤1 µg/mL)	S based on CLSI, NS by FDA breakpoints (MIC=2–4 µg/mL)	NS by FDA and CLSI breakpoints (MIC=8–16 µg/mL)
Clinical response	N=29	N=13	N=4
Yes	20 (69)	9 (69)	4 (100)
No	4 (14)	2 (15)	
Not reported	5 (17)	2 (15)	
Known vital status	N=26	N=12	N=not provided
Day 28 mortality	6 (23.1%)	4 (33.3%)	0 (0%)

Abbreviations: CLSI, Clinical and Laboratory Standards Institute; FDA, US Food and Drug Administration; MIC, minimum inhibitory concentration; NS, non-susceptible; S, susceptible.
Table adapted from Satlin et al. *Antimicrob Agents Chemother*. 2023.

- AEs were reported in 19 (41%) patients
  - The AEs were related or possibly related to cefiderocol for 3 patients (n=1 each)
    - Increased liver enzymes (confounded by liver transplant and hepatic abscesses following surgery) which resolved following cefiderocol discontinuation
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Surveillance Studies

Kimbrough et al (2025) evaluated the *in vitro* activity of cefiderocol and various BL–BLI combinations against *P. aeruginosa* isolates collected as part of the SENTRY Antimicrobial Surveillance Program. A total of 9572 clinical *P. aeruginosa* isolates were collected from hospitalized patients across 36 US (n=4400) and 43 primarily European hospitals (n=5172) between 2020 and 2023.[12]

- MICs were determined according to CLSI guidelines using broth microdilution with ID-CAMHB for cefiderocol and CAMHB for comparator agents. Susceptibility to cefiderocol was evaluated according to CLSI, EUCAST, and FDA criteria (all 2025), while susceptibility was interpreted using CLSI (2025) criteria for all BL–BLI combinations tested
- DTR phenotypes were defined by NS MIC results (according to CLSI breakpoints) to piperacillin–tazobactam, ceftazidime, cefepime, aztreonam, meropenem, imipenem, ciprofloxacin, and levofloxacin

Results[12]

- Overall, 98.6–99.8% (depending on breakpoint chosen) of *P. aeruginosa* isolates were shown to be susceptible to cefiderocol – see **Table 10**
  - 96.1%, 96.5%, and 95.9% were susceptible to ceftazidime–avibactam, imipenem–relebactam, and ceftolozane–tazobactam, respectively
- A DTR phenotype was identified in 377 the *P. aeruginosa* isolates (3.9% of the entire collection), and cefiderocol retained activity in 88.9–98.1% of cases – see **Table 10**
  - By contrast, the 3 BL–BLI combinations tested demonstrated lower activity against this subset of isolates with a susceptibility range of 52.3–56%
- Among DTR isolates NS to ≥1 of the 3 tested BL–BLI combinations, cefiderocol (82–97.5%) maintained consistent MIC_{50} and MIC_{90} values of 0.25 mg/L and 2 mg/L, respectively – see **Table 10**
  - Susceptibility was low (≤30.3%) for the 3 tested BL–BLI combinations when non-susceptibility was demonstrated among them
  - Cefiderocol also maintained activity against DTR isolates NS to any 2 or all 3 of the BL–BLI combinations tested (79.3–96.3%), whereas susceptibilities of the BL–BLI combinations were 0–18.5%

Table 10. Activity of Cefiderocol and Comparator BL–BLI Combinations Tested against *P. aeruginosa* Isolates Collected from US and European Medical Centers (2020–2023)[12]

Susceptibility Profile n (%)	Susceptibility (%)						
	CZA	I/R	TOL/TAZ	Cefiderocol			Cefiderocol
	CLSI (%)			CLSI (%)	EUCAST (%)	FDA (%)	$MIC_{50/90}$ (mg/L)
All Isolates 9572 (100)	96.1	96.5	95.9	99.8	99.5	98.6	0.12/0.25
DTR 377 (3.9)	52.3	56	54.4		96.8	88.9	0.12/2
BL–BLI-NS[a] 238 (63.1)	24.4	30.3			95.8	85.7	0.25/2
CZA-NS 180 (47.7)		29.4			95	83.9	0.25/2
I/R-NS 166 (44)	23.5				95.8	86.7	0.25/2
TOL/TAZ-NS 172 (45.6)	21.5	25.6			94.8	82	0.25/2
CZA/I/R-NS 127 (33.6)			13.4		94.5	84.3	0.25/2
CZA/TOL/TAZ-NS 135 (35.8)		18.5			94.1	79.3	0.25/2
I/R/TOL/TAZ-NS 128 (34)	14.1				94.5	84.4	0.25/2
CZA/I/R/TOL/TAZ-NS 110 (29.2)					93.6	81.8	0.25/2

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Surveillance Studies

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Susceptibility Profile n (%)	Susceptibility (%)						
	CZA	I/R	TOL/TAZ	Cefiderocol			Cefiderocol
	CLSI (%)			CLSI (%)	EUCAST (%)	FDA (%)	$MIC_{50/90}$ (mg/L)
All Isolates 9572 (100)	96.1	96.5	95.9	99.8	99.5	98.6	0.12/0.25
DTR 377 (3.9)	52.3	56	54.4	98.1	96.8	88.9	0.12/2
BL–BLI-NS[a] 238 (63.1)	24.4	30.3	27.7	97.5	95.8	85.7	0.25/2
CZA-NS 180 (47.7)		29.4	25	97.2	95	83.9	0.25/2
I/R-NS 166 (44)	23.5		22.9	97	95.8	86.7	0.25/2
TOL/TAZ-NS 172 (45.6)	21.5	25.6		96.5	94.8	82	0.25/2
CZA/I/R-NS 127 (33.6)			13.4	96.1	94.5	84.3	0.25/2
CZA/TOL/TAZ-NS 135 (35.8)		18.5		96.3	94.1	79.3	0.25/2
I/R/TOL/TAZ-NS 128 (34)	14.1			96.1	94.5	84.4	0.25/2
CZA/I/R/TOL/TAZ-NS 110 (29.2)				95.5	93.6	81.8	0.25/2

Abbreviations: BL–BLI, β-lactam–β-lactamase inhibitor; CZA, ceftazidime–avibactam; CLSI, Clinical and Laboratory Standards Institute; DTR, difficult-to-treat; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FDA, US Food and Drug Administration; I/R, imipenem–relebactam; MIC, minimum inhibitory concentration; NS, non-susceptible; TOL/TAZ, ceftolozane–tazobactam.
[a]Isolates that were NS to ≥1 of the BL–BLI combination agents CZA, I/R, or TOL/TAZ.
Table adapted from Kimbrough et al. *Microbiol Spectr*. 2025.

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Surveillance Studies (Cont.)

Results (Cont.)[12]

- Table 11 shows the activity of cefiderocol and comparator anti-pseudomonal agents (both single and combination) against the DTR and non-DTR subsets of *P. aeruginosa* isolates
- DTR isolates with carbapenemase genes were identified in 74 (19.6%) cases, (class B MBL-type being the most commonly detected)
  - Cefiderocol retained activity against both non-carbapenemase and carbapenemase-carrying isolates (and respective subsets) with a susceptibility range of 82.6–100% – see Table 12
  - By contrast, the 3 tested BL–BLI combinations were almost completely inactive against the carbapenemase-carrying subsets and showed limited activity against the non-carbapenemase group (susceptibility ranging from 63.7–69.6%)
  - Among carbapenemase-carrying DTR isolates, 70 (94.6%) were NS to all 3 tested BL–BLI combinations, while cefiderocol remained active against these isolates (susceptibility range: 82.9–97.1%)

Table 11. Activity of Cefiderocol and Comparator BL–BLI Combinations Tested against DTR and non-DTR *P. aeruginosa* Isolates Collected from US and European Medical Centers (2020–2023)[12]

Organism Group / Antimicrobial Agent	MIC (mg/L) 50%	MIC (mg/L) 90%	MIC (mg/L) Range	CLSI S (%)	CLSI R (%)	EUCAST S (%)	EUCAST R (%)	FDA S (%)	FDA R (%)
DTR (377)									
Cefiderocol	0.12	2	≤0.004 to >64	98.1	1.1	96.8	3.2	88.9	3.2
Ceftazidime–avibactam	8	>32	1 to >32	52.3	47.7	52.3	47.7	52.3	47.7
Imipenem–relebactam	2	>8	0.25 to >8	56	29.4	56	44	56	29.4
Ceftolozane–tazobactam	4	>16	1 to >16	54.4	34.7	54.4	45.6	54.4	34.7
Aztreonam–avibactam	>16	>16	0.5 to >16						
Piperacillin–tazobactam	128	>128	32 to >128	0	88.9	[a]	100	0	100
Ceftazidime	>32	>32	16 to >32	0	86.7	[a]	100	0	100
Cefepime	32	>32	16 to >32	0	57.3	[a]	100	0	100
Meropenem	16	>32	4 to >32	0	94.2	0[b]	74.3	0	94.2
Imipenem	>8	>8	4 to >32	0	93.1	[a]	93.1	0	93.1
Aztreonam	>16	>16	16 to >32	0	81.4	[a]	81.4	0	81.4
Ciprofloxacin	>4	>4	2 to >4	0	85.1	[a]	100	0	85.1
Levofloxacin	16	>32	8 to >32	0	95.8	[a]	95.8	0	95.8
Colistin	0.5	1	≤0.06 to >8		0.3	99.7	0.3		
Non-DTR (9195)									
Cefiderocol	0.12	0.25	≤0.004 to >64	99.6	0.1	99.6	0.4	99	0.4
Ceftazidime–avibactam	2	4	≤0.06 to >32	97.9	2.1	97.9	2.1	97.9	2.1
Imipenem–relebactam	0.25	1	≤0.03 to >32	98.9	1.1	98.1	1.9	98.1	1.1
Ceftolozane–tazobactam	0.5	2	≤0.12 to >16	97.6	1.5	97.6	2.4	97.6	1.5
Aztreonam–avibactam	4	16	≤0.03 to >16						
Piperacillin–tazobactam	4	64	≤0.06 to >128	82.6	11.7	[a]	17.4	72.4	17.4
Ceftazidime	2	16	0.06 to >32	86.4	9.9	[a]	13.6	86.4	13.6
Cefepime	2	16	0.06 to >32	89.4	3.2	[a]	10.6	89.4	10.6
Meropenem	0.5	8	≤0.015 to >32	83.6	10.8	83.6[b]	5.9	83.6	10.8
Imipenem	1	8	≤0.12 to >8	81.6	14.4	[a]	14.4	81.6	14.4
Aztreonam	8	>16	0.06 to >16	75	15	[a]	15	75	15
Ciprofloxacin	0.12	2	≤0.008 to >4	84.1	11.2	[a]	15.9	84.1	11.2
Levofloxacin	0.5	4	≤0.015 to >32	75.5	14.7	[a]	14.7	75.5	14.7
Colistin	0.5	1	≤0.06 to >8		0.4	99.8	0.2		

Table 12. Activity of Cefiderocol and Comparator BL–BLI Combinations Tested against DTR *P. aeruginosa* Isolates with Carbapenemase Genes Collected from US and European Medical Centers (2020–2023)[12]

Genotype n (%)	Susceptibility (%) CZA	I/R	TOL/TAZ	Cefiderocol CLSI (%)	Cefiderocol EUCAST (%)	Cefiderocol FDA (%)	Cefiderocol $MIC_{50/90}$ (mg/L)
	CLSI (%)						
Non-Carbapenemase[a] 303 (80.4)	63.7	69.6	67.7	98.3	97.4	90.1	0.12/1
Carbapenemase[b] 74 (19.6)	5.4	0			94.6	83.8	0.25/2
MBL 69 (93.2)	0	0			94.2	82.6	0.25/2
VIM 53 (71.6)	0	0			98.1	88.7	0.25/2
Carbapenemase+BL–BLI-NS[c] 70 (18.6)	0	0	0	97.1	94.3	82.9	0.25/2

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Surveillance Studies (Cont.)

Table 11. Activity of Cefiderocol and Comparator BL–BLI Combinations Tested against DTR and non-DTR *P. aeruginosa* Isolates Collected from US and European Medical Centers (2020–2023)[12]

Organism Group / Antimicrobial Agent	MIC (mg/L)			CLSI		EUCAST		FDA	
	50%	90%	Range	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)
DTR (377)									
Cefiderocol	0.12	2	≤0.004 to >64	98.1	1.1	96.8	3.2	88.9	3.2
Ceftazidime–avibactam	8	>32	1 to >32	52.3	47.7	52.3	47.7	52.3	47.7
Imipenem–relebactam	2	>8	0.25 to >8	56	29.4	56	44	56	29.4
Ceftolozane–tazobactam	4	>16	1 to >16	54.4	34.7	54.4	45.6	54.4	34.7
Aztreonam–avibactam	>16	>16	0.5 to >16						
Piperacillin–tazobactam	128	>128	32 to >128	0	88.9	[a]	100	0	100
Ceftazidime	>32	>32	16 to >32	0	86.7	[a]	100	0	100
Cefepime	32	>32	16 to >32	0	57.3	[a]	100	0	100
Meropenem	16	>32	4 to >32	0	94.2	0[b]	74.3	0	94.2
Imipenem	>8	>8	4 to >8	0	93.1	[a]	93.1	0	93.1
Aztreonam	>16	>16	16 to >16	0	81.4	[a]	81.4	0	81.4
Ciprofloxacin	>4	>4	1 to >4	0	85.1	[a]	100	0	85.1
Levofloxacin	16	>32	2 to >32	0	95.8	[a]	95.8	0	95.8
Colistin	0.5	1	≤0.06 to >8		0.3	99.7	0.3		
Non-DTR (9195)									
Cefiderocol	0.12	0.25	≤0.004 to 32	99.8	0.1	99.6	0.4	99	0.4
Ceftazidime–avibactam	2	4	≤0.015 to >32	97.9	2.1	97.9	2.1	97.9	2.1
Imipenem–relebactam	0.25	1	≤0.03 to >8	98.1	1.1	98.1	1.9	98.1	1.1
Ceftolozane–tazobactam	0.5	2	≤0.12 to >16	97.6	1.5	97.6	2.4	97.6	1.5
Aztreonam–avibactam	4	16	≤0.03 to >16						
Piperacillin–tazobactam	4	64	≤0.06 to >128	82.6	11.7	[a]	17.4	72.4	17.4
Ceftazidime	2	16	0.06 to >32	86.4	9.9	[a]	13.6	86.4	13.6
Cefepime	2	16	0.06 to >32	89.4	3.2	[a]	10.6	89.4	10.6
Meropenem	0.5	8	≤0.015 to >32	83.6	10.8	83.6[b]	5.9	83.6	10.8
Imipenem	1	8	≤0.12 to >8	81.6	14.4	[a]	14.4	81.6	14.4
Aztreonam	8	>16	0.06 to >16	75	15	[a]	15	75	15
Ciprofloxacin	0.12	2	≤0.008 to >4	84.1	11.2	[a]	15.9	84.1	11.2
Levofloxacin	0.5	4	≤0.015 to >32	75.5	14.7	[a]	14.7	75.5	14.7
Colistin	0.5	1	≤0.06 to >8		0.4	99.8	0.2		

Abbreviations: BL–BLI, β-lactam–β-lactamase inhibitor; CLSI, Clinical and Laboratory Standards Institute; DTR, difficult-to-treat; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FDA, US Food and Drug Administration; MIC, minimum inhibitory concentration; NS, non-susceptible; R, resistant; S, susceptible.

[a]Intermediate results can be considered susceptible if increased antibiotic exposures can be achieved.

[b]Using non-meningitis breakpoints.

Table adapted from Kimbrough et al. *Microbiol Spectr*. 2025.

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Surveillance Studies (Cont.)

Table 12. Activity of Cefiderocol and Comparator BL–BLI Combinations Tested against DTR *P. aeruginosa* Isolates with Carbapenemase Genes Collected from US and European Medical Centers (2020–2023)[12]

Genotype n (%)	Susceptibility (%)						
	CZA	I/R	TOL/TAZ	Cefiderocol			Cefiderocol
	CLSI (%)			CLSI (%)	EUCAST (%)	FDA (%)	$MIC_{50/90}$ (mg/L)
Non-Carbapenemase[a] 303 (80.4)	63.7	69.6	67.7	98.3	97.4	90.1	0.12/1
Carbapenemase[b] 74 (19.6)	5.4	0	0	97.3	94.6	83.8	0.25/2
MBL 69 (93.2)	0	0	0	97.1	94.2	82.6	0.25/2
VIM 53 (71.6)	0	0	0	100	98.1	88.7	0.25/2
Carbapenemase+BL–BLI-NS[c] 70 (18.6)	0	0	0	97.1	94.3	82.9	0.25/2

Abbreviations: BL–BLI, β-lactam–β-lactamase inhibitor; CZA, ceftazidime–avibactam; CLSI, Clinical and Laboratory Standards Institute; DTR, difficult-to-treat; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FDA, US Food and Drug Administration; I/R, imipenem–relebactam; MBL, metallo-β-lactamase; MIC, minimum inhibitory concentration; NS, non-susceptible; TOL/TAZ, ceftolozane–tazobactam; VIM, Verona integron-mediated metallo-β-lactamase.

[a]Includes isolates where acquired carbapenemases were not detected.

[b]Includes isolates with bla_{GES-4} (1), bla_{GES-5} (1), bla_{GES-6} (3), bla_{IMP-1} (2), bla_{IMP-7} (5), bla_{IMP-8} (1), bla_{IMP-13} (1), bla_{NDM-1} (7), bla_{VIM-1} (6), bla_{VIM-1} + bla_{HMB-1} (1), bla_{VIM-2} (41), bla_{VIM-2} + bla_{GES-5} (1), bla_{VIM-4} (3), and bla_{VIM-5} (1).

[c]Includes isolates NS (CLSI) to the 3 BL–BLI combinations and carrying acquired carbapenemases, as follows: bla_{GES-4} (1), bla_{IMP-1} (2), bla_{IMP-7} (5), bla_{IMP-8} (1), bla_{IMP-13} (1), bla_{NDM-1} (7), bla_{VIM-1} (6), bla_{VIM-1} + bla_{HMB-1} (1), bla_{VIM-2} (41), bla_{VIM-2} + bla_{GES-5} (1), bla_{VIM-4} (3), and bla_{VIM-5} (1).

Table adapted from Kimbrough et al. *Microbiol Spectr*. 2025.

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Surveillance Studies (Cont.)

Mendes et al (2025) examined the *in vitro* activity of cefiderocol and comparator agents against *P. aeruginosa* isolates (including resistant subsets), collected from US hospitals during the SENTRY Antimicrobial Surveillance Program (2020–2024)[13]

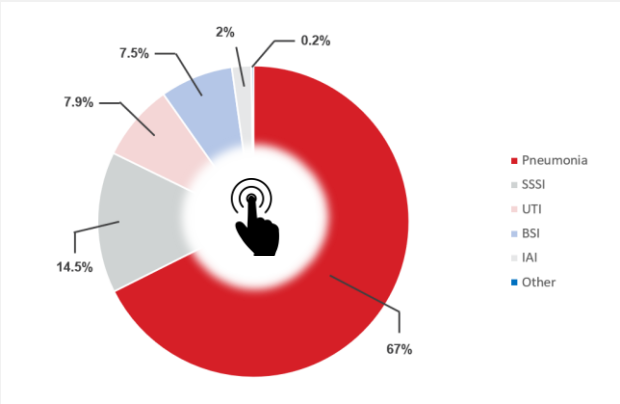
Methods[13]

- A total of 5478 consecutive *P. aeruginosa* isolates were cultured from patients hospitalized across 38 medical centers in all 9 US Census Divisions between 2020 and 2024
- MIC values were determined in accordance with CLSI guidelines by broth microdilution using ID-CAMHB for cefiderocol alone, and CAMHB for all other comparator agents
  - MIC results for cefiderocol were interpreted according to both CLSI and FDA (2025) criteria, whereas comparator agent MIC values were interpreted using CLSI breakpoints
- Screening of β-lactamase genes was done by preparing DNA libraries from total genomic DNA extracted from all *P. aeruginosa* isolates, before alignment of assembled sequences against an in-house database of known β-lactamase genes

Results[13]

- Of the total collection of *P. aeruginosa* isolates (N=5478), 805 (14.7%) were classified as MDR, 190 (3.5%) were DTR, and 116 (2.1%) were XDR
- 1238 (22.6%) were classed as Carb-NS, and 98.9% of those isolates were carbapenemase-negative
  - The most frequent Carb-NS *P. aeruginosa* infection sites were pneumonia (67%), SSSIs (14.5%), BSIs (7.5%), and UTIs (7.9%) – see **Figure 4**

Figure 4. Infection Type Distribution Resulting from Carb-NS *P. aeruginosa* Infection[13]

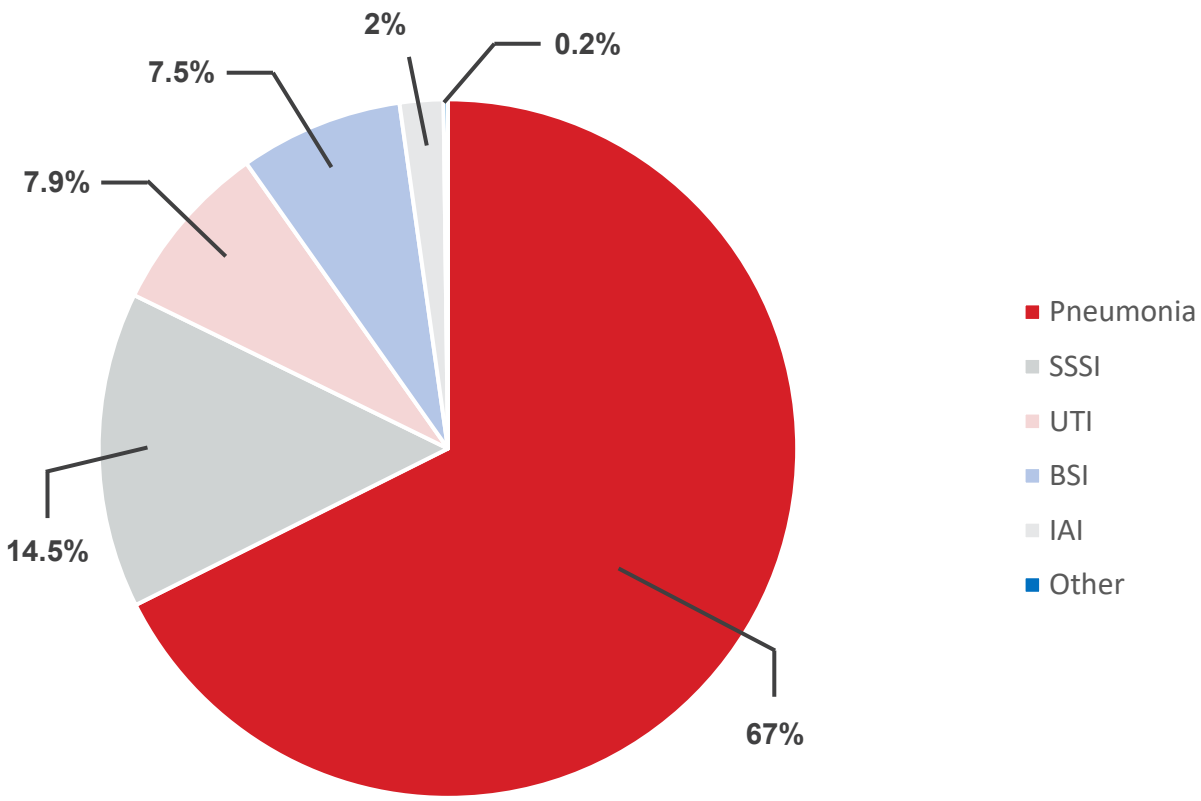


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Surveillance Studies (Cont.)

Figure 4. Infection Type Distribution Resulting from Carb-NS *P. aeruginosa* Infection[13]



Abbreviations: BSI, bloodstream infections; IAI, intra-abdominal infection; SSSI, skin and skin structure infections; UTI, urinary tract infection.
Figure adapted from Mendes et al. IDWeek. 2025.

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Surveillance Studies (Cont.)

Results (Cont.)[13]

- Overall, cefiderocol and comparator agents exhibited susceptibilities >95% against all *P. aeruginosa*, with the exception of piperacillin–tazobactam (79.4% susceptible) – see Table 13
- Against MDR *P. aeruginosa* isolates, cefiderocol had a $MIC_{50/90}$ of 0.12/0.5 mg/L (95.5–99.1% susceptible), while cefiderocol was also capable of inhibiting 91.6–98.4% and 88.8–96.6% of DTR ($MIC_{50/90}$, 0.12/1 mg/L), and XDR ($MIC_{50/90}$, 0.12/2 mg/L) *P. aeruginosa* isolates, respectively – see Table 13
  - By contrast, BL–BLI combinations showed lower susceptibility levels (≤85.1% susceptible) against the MDR, DTR, and XDR isolate subsets
- Of the agents tested, cefiderocol had the lowest MIC (96.8–99.4% susceptible) against Carb-NS *P. aeruginosa* (a MIC_{90} ≥4-fold lower than all comparator agents) – see Table 13
  - Imipenem–relebactam, ceftazidime–avibactam, and ceftolozane–tazobactam had susceptibilities of 87.1–90.1%, respectively
- Cefiderocol was shown to inhibit all *P. aeruginosa* isolates carrying carbapenemase genes at ≤2 mg/L (eg, 100% susceptibility) – see Table 13
  - By contrast, the maximum susceptibility of any of the comparator agents was 23.1%

Table 13. Activity of Cefiderocol and BL–BLI Comparator Agents against *P. aeruginosa* Isolates and Specific Resistant Subsets[13]

Phenotype/Genotype[a] (number tested)	$MIC_{50/90}$ in mg/L (% Susceptible by CLSI/FDA Criteria)[b]					
	Cefiderocol	Imipenem–relebactam	Ceftazidime–avibactam	Ceftolozane–tazobactam	Piperacillin–tazobactam	Meropenem
All (5478)	0.12/0.25 (99.8/98.6)	0.25/1 (97.8)	2/8 (96.6)	0.5/2 (97.4)	8/128 (79.4)	0.5/8 (81.2)
MDR (805)	0.12/0.5 (99.1/95.5)	1/4 (85.1)	8/16 (78.6)	2/8 (83.9)	128/>128 (11.1)	8/32 (18)
DTR (190)	0.12/1 (98.4/91.6)	2/8 (65	)	4/>16 (70.5)	>128/>128 (0)	16/32 (0)
XDR (116)	0.12/2 (96.6/88.8)	4/>8 (24	)	4/>16 (59.5)	128/>128 (2.6)	16/>32 (0)
Carb-NS (1238)	0.12/0.5 (99.4/96.8)	1/2 (90.1)	4/16 (87.1)	1/4 (90.1)	32/>128 (49.3)	8/32 (16.6)
Carbapenemase-(+)[b] (13)	0.5/2 (100/84.6)	>8/>8 (23.1)	>32/>32 (23.1)	>16/>16 (7.7)	128/>128 (15.4)	>32/>32 (0)
Carbapenemase-(–) (1225)	0.12/0.5 (99.4/97)	1/2 (90.8)	4/16 (87.8)	1/4 (91)	32/>128 (49.7)	8/32 (16.8)

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Surveillance Studies (Cont.)

Table 13. Activity of Cefiderocol and BL–BLI Comparator Agents against *P. aeruginosa* Isolates and Specific Resistant Subsets[13]

Phenotype/Genotype[a] (number tested)	$MIC_{50/90}$ in mg/L (% Susceptible by CLSI/FDA Criteria)[b]					
	Cefiderocol	Imipenem–relebactam	Ceftazidime–avibactam	Ceftolozane–tazobactam	Piperacillin–tazobactam	Meropenem
All (5478)	0.12/0.25 (99.8/98.6)	0.25/1 (97.8)	2/8 (96.6)	0.5/2 (97.4)	8/128 (79.4)	0.5/8 (81.2)
MDR (805)	0.12/0.5 (99.1/95.5)	1/4 (85.1)	8/16 (78.6)	2/8 (83.9)	128/>128 (11.1)	8/32 (18)
DTR (190)	0.12/1 (98.4/91.6)	2/8 (65.3)	8/32 (61.6)	4/>16 (70.5)	>128/>128 (0)	16/32 (0)
XDR (116)	0.12/2 (96.6/88.8)	4/>8 (24.1)	8/>32 (56)	4/>16 (59.5)	128/>128 (2.6)	16/>32 (0)
Carb-NS (1238)	0.12/0.5 (99.4/96.8)	1/2 (90.1)	4/16 (87.1)	1/4 (90.1)	32/>128 (49.3)	8/32 (16.6)
Carbapenemase-(+)[b] (13)	0.5/2 (100/84.6)	>8/>8 (23.1)	>32/>32 (23.1)	>16/>16 (7.7)	128/>128 (15.4)	>32/>32 (0)
Carbapenemase-(–) (1225)	0.12/0.5 (99.4/97)	1/2 (90.8)	4/16 (87.8)	1/4 (91)	32/>128 (49.7)	8/32 (16.8)

Abbreviations: CLSI, Clinical and Laboratory Standards Institute; DTR, difficult-to-treat resistant; FDA, US Food and Drug Administration; GES, Guiana extended-spectrum β-lactamase; IMP, imipenemase; KPC, *Klebsiella pneumoniae* carbapenemase; MDR, multidrug resistant; $MIC_{50/90}$, minimum inhibitory concentration at which 50% and 90% of isolates are inhibited; NDM, New Delhi metallo-β-lactamase; NS, non-susceptible; VIM, Verona integron-encoded metallo-β-lactamase; XDR, extensively drug resistant.

[a]MDR classified as NS (CLSI breakpoints) to ≥3 drug classes; DTR defined as NS (CLSI) to piperacillin–tazobactam, ceftazidime, cefepime, aztreonam, meropenem, imipenem, ciprofloxacin, and levofloxacin; XDR defined as NS (CLSI) to all but 2 or fewer drug classes; Carb-NS isolates NS (MIC values ≥4 mg/L) to imipenem and/or meropenem based on CLSI criteria.

[b]Cefiderocol MIC results were interpreted according to the CLSI/FDA criteria, whereas comparator agent MIC values were interpreted based on CLSI criteria.

[c]Includes bla_{GES-5} (2), bla_{IMP-1} (1), bla_{IMP-13} (1), bla_{IMP-83} (1), bla_{KPC-2} (1), bla_{NDM-1} (2), bla_{VIM-1} (1), and bla_{VIM-2} (4).

Table adapted from Mendes et al. IDWeek. 2025.

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Surveillance Studies (Cont.)

Yamano et al (2025) tracked the *in vitro* activity of cefiderocol over a 5-year period against Gram-negative bacterial isolates collected from hospitalized patients across the US and Europe during the SENTRY Antimicrobial Surveillance Program between 2020 and 2024.[14]

Methods[14]

- Of the 60,582 clinical isolates, a total of 11,757 were *P. aeruginosa* – see **Figure 5**
- MICs for cefiderocol were determined using broth microdilution with ID-CAMHB according to CLSI guidelines, while %S to cefiderocol and carbapenems were defined using 2025 CLSI breakpoints
- %S to cefiderocol over a 5-year period was determined for *P. aeruginosa* isolates, including carbapenem (meropenem or imipenem)-resistant or -NS subsets, in both the US and Europe

Results[14]

- Consistently high activity was observed for cefiderocol against *P. aeruginosa* isolates over the 5-year study period – see **Figure 6**
- %S was 98.8–100% for all *P. aeruginosa* isolates, and 95.3–100% for the Carb-NS subsets
  - The lowest observed %S (95.3%) was for Carb-NS *P. aeruginosa* isolates in Europe in 2024

Figure 5. Trends in (A) Total Number and (B) Carb-NS *P. aeruginosa* Isolates Over 5 Years of the SENTRY Surveillance Program (2020–2024)[14]

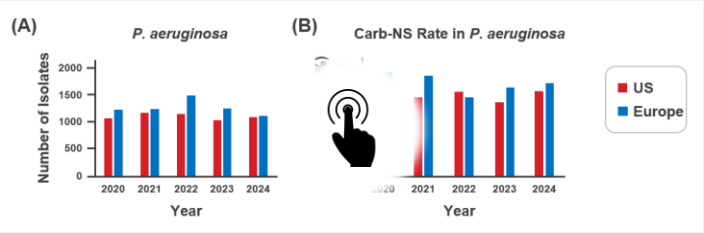
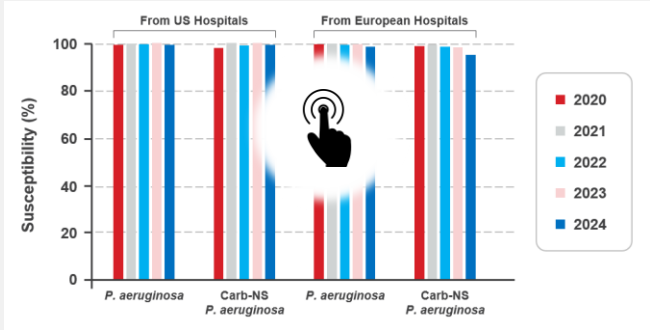


Figure 6. Susceptibility to Cefiderocol by Year of *P. aeruginosa* Isolates Collected from US and European Hospitals during the SENTRY Surveillance Program (2020–2024)[14]

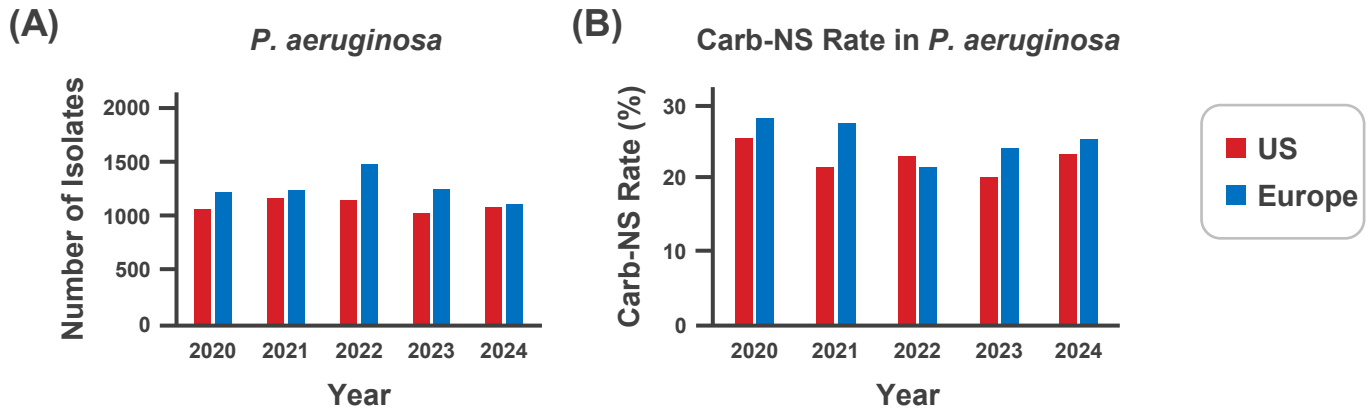


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Surveillance Studies (Cont.)

Figure 5. Trends in (A) Total Number and (B) Carb-NS *P. aeruginosa* Isolates Over 5 Years of the SENTRY Surveillance Program (2020–2024)[14]



Abbreviations: Carb-NS, carbapenem non-susceptible; US, United States.
Figure adapted from Yamano et al. IDWeek. 2025.

Figure 5. Trends in (A) Total Number and (B) Carb-NS *P. aeruginosa* Isolates Over 5 Years of the SENTRY Surveillance Program (2020–2024)[14]

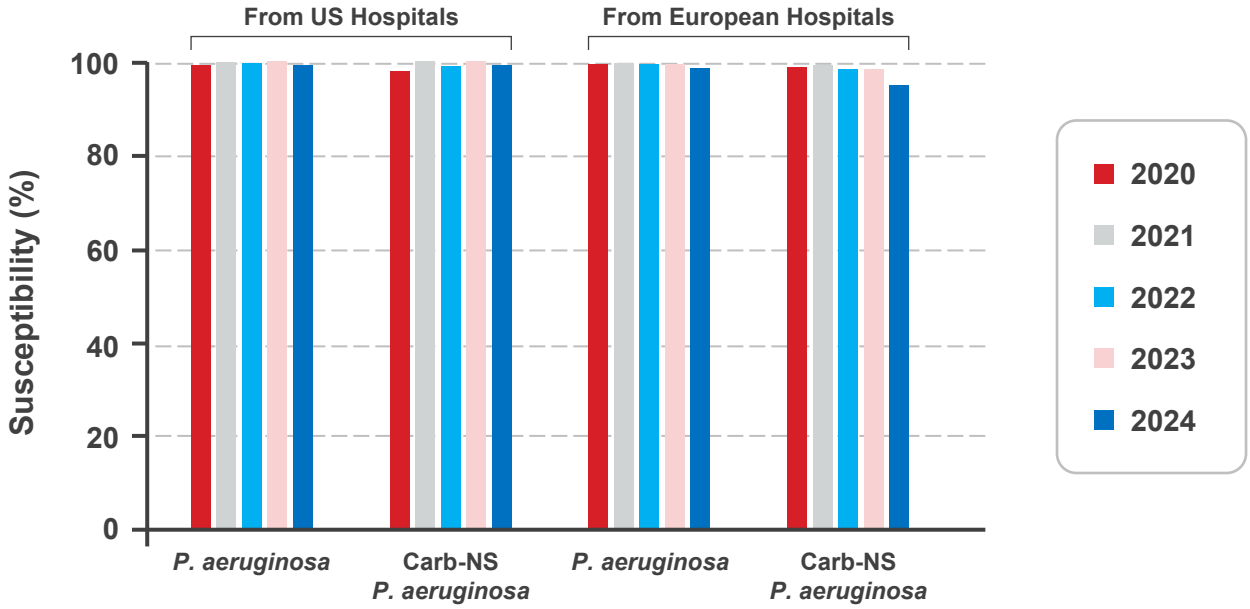
Figure 6. Susceptibility to Cefiderocol by Year of *P. aeruginosa* Isolates Collected from US and European Hospitals during the SENTRY Surveillance Program (2020–2024)[14]

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Surveillance Studies (Cont.)

Figure 6. Susceptibility to Cefiderocol by Year of *P. aeruginosa* Isolates Collected from US and European Hospitals during the SENTRY Surveillance Program (2020–2024)[14]



Abbreviations: Carb-NS, carbapenem non-susceptible; US, United States.
Figure adapted from Yamano et al. IDWeek. 2025.

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Surveillance Studies (Cont.)

DeJonge et al (2025) assessed the potential degree of cross resistance to cefiderocol and various BL–BLI combinations in Gram-negative bacterial isolates collected from hospitalized patients across the US and Europe during the SENTRY Antimicrobial Surveillance Program between 2020 and 2024.[15]

Methods[15]

- 11,757 *P. aeruginosa* isolates were collected in total
- MICs for cefiderocol were determined using broth microdilution with ID-CAMHB according to CLSI guidelines for cefiderocol, and with CAMHB for the various BL–BLI combinations
- Assessment of susceptibility to cefiderocol was determined according to the 2025 CLSI, EUCAST and FDA breakpoints, while susceptibility to the BL–BLI combinations was assessed using CLSI breakpoints

Results[15]

- Overall, 4.2%, 4.1%, and 3.5% of *P. aeruginosa* isolates were determined to be NS to ceftolozane–tazobactam, ceftazidime–avibactam, and imipenem–relebactam, respectively, although these percentages appeared to show an upward trend over the study period – see **Figure 7**
  - Prevalence of non-susceptibility was consistently higher in isolates from European hospitals versus those collected from US hospitals – see **Figure 8**

Figure 7. Prevalence of *P. aeruginosa* Isolates NS to BL–BLI Combinations during Study Period[15]

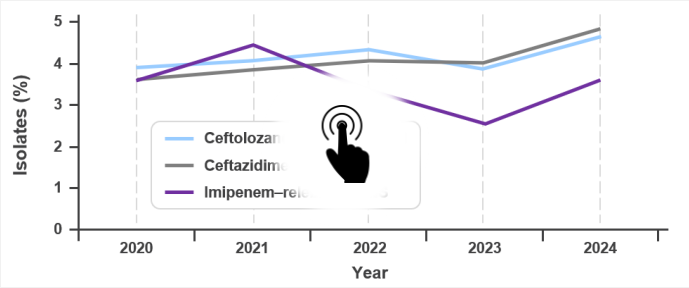
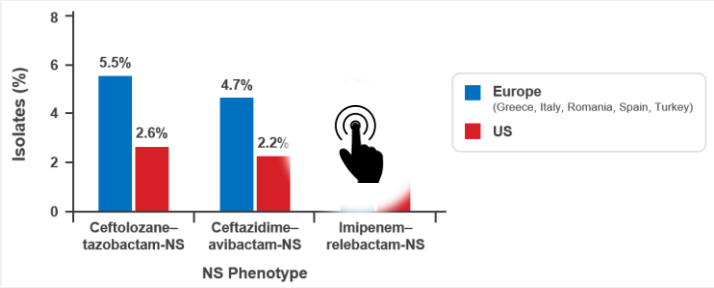


Figure 8. Prevalence of *P. aeruginosa* Isolates NS to BL–BLI Combinations by Region[15]



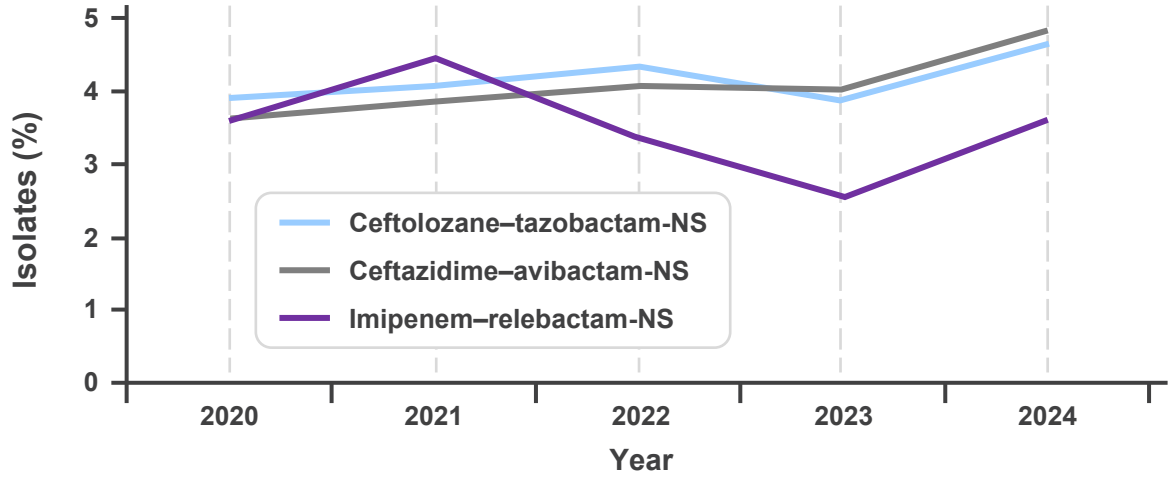
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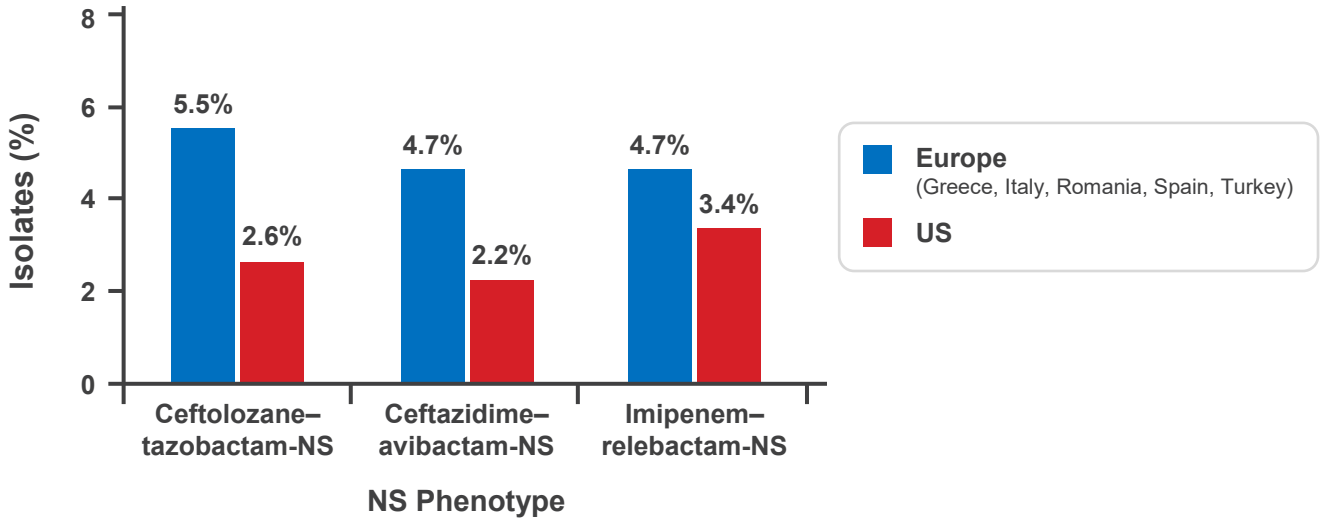
Surveillance Studies (Cont.)

Figure 7. Prevalence of *P. aeruginosa* Isolates NS to BL–BLI Combinations during Study Period[15]



Abbreviations: BL–BLI, β-lactam–β-lactamase inhibitor; NS, non-susceptible.
Figure adapted from DeJonge et al. IDWeek. 2025.

Figure 8. Prevalence of *P. aeruginosa* Isolates NS to BL–BLI Combinations by Region[15]



Abbreviations: BL–BLI, β-lactam–β-lactamase inhibitor; NS, non-susceptible.
Figure adapted from DeJonge et al. IDWeek. 2025.

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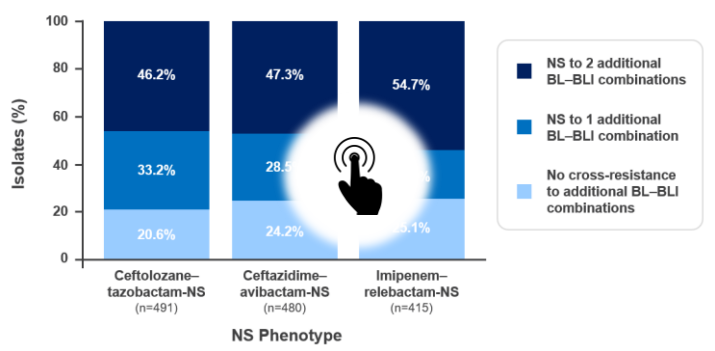
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Surveillance Studies (Cont.)

Results (Cont.)[15]

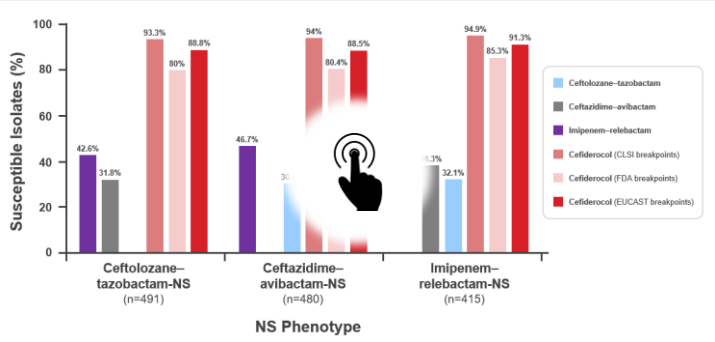
- The majority of *P. aeruginosa* isolates were NS to other BL–BLI combinations – see **Figure 9**

Figure 9. Cross-Resistance among BL–BLI Combinations against *P. aeruginosa* Isolates in the SENTRY Antimicrobial Surveillance Program (2020–2024)[15]



- Cefiderocol retained activity against *P. aeruginosa* isolates NS to BL–BLI combinations – see **Figure 10**

Figure 10. Cefiderocol Susceptibility of *P. aeruginosa* Isolates NS to BL–BLI Combinations in the SENTRY Antimicrobial Surveillance Program (2020–2024)[15]

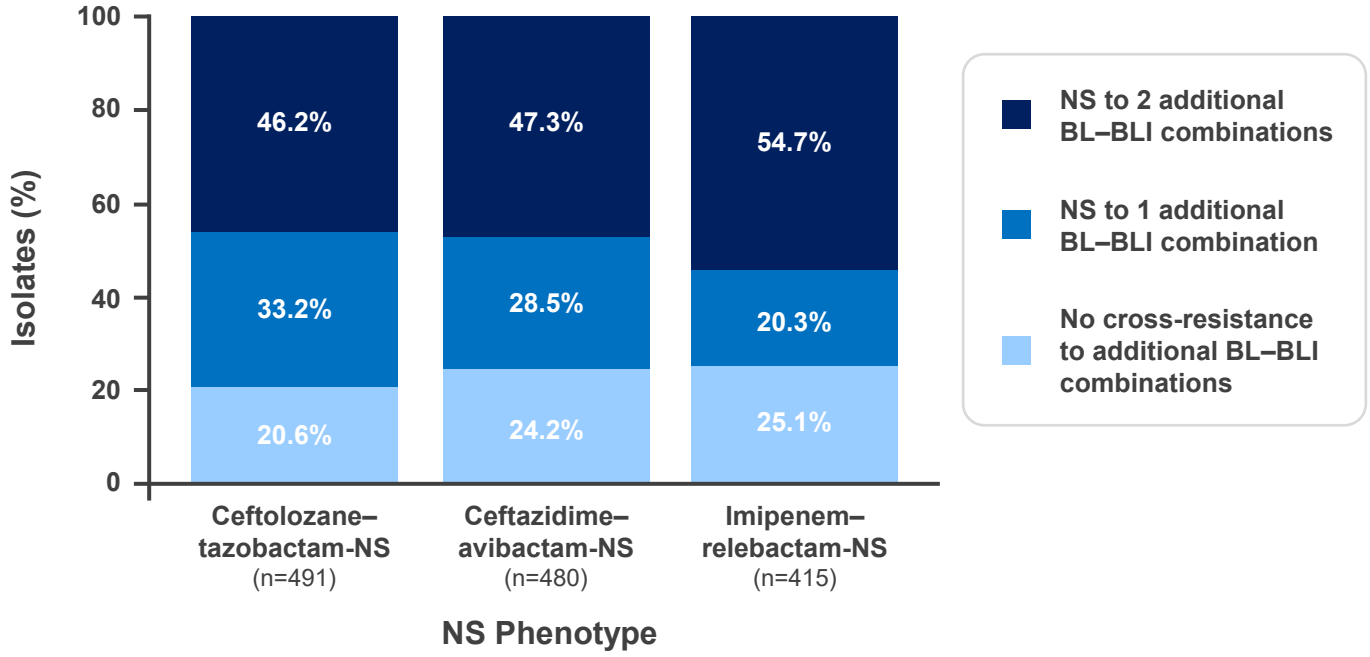


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Surveillance Studies (Cont.)

Figure 9. Cross-Resistance among BL–BLI Combinations against *P. aeruginosa* Isolates in the SENTRY Antimicrobial Surveillance Program (2020–2024)[15]



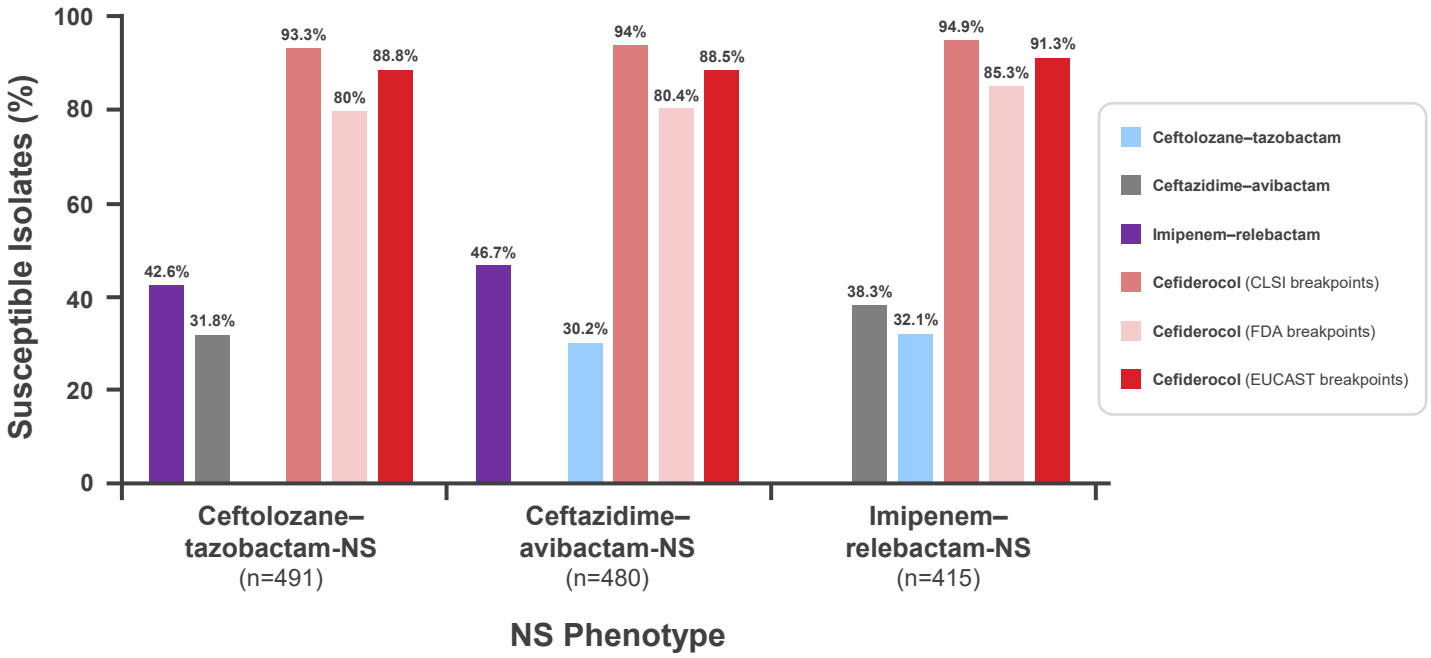
Abbreviations: BL–BLI, β-lactam–β-lactamase inhibitor; NS, non-susceptible.
Figure adapted from DeJonge et al. IDWeek. 2025.

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Surveillance Studies (Cont.)

Figure 10. Cross-Resistance among BL–BLI Combinations against *P. aeruginosa* Isolates in the SENTRY Antimicrobial Surveillance Program (2020–2024)[15]



Abbreviations: BL–BLI, β-lactam–β-lactamase inhibitor; CLSI, Clinical and Laboratory Standards Institute; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FDA, US Food and Drug Administration; NS, non-susceptible.
Figure adapted from DeJonge et al. IDWeek. 2025.

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Surveillance Studies (Cont.)

Mendes et al (2024) evaluated the *in vitro* activity of cefiderocol and comparator agents against *P. aeruginosa* isolates carrying MBL genes that had been collected in the US and Europe between 2020–2023 as part of the SENTRY Antimicrobial Surveillance Program.[16]

Methods[16]

- 9572 *P. aeruginosa* isolates were collected from hospitalized patients from 36 medical centers in the US and 43 sites across Europe (including Turkey and Israel) between 2020 and 2023
- MICs and susceptibility were determined according to CLSI criteria using broth microdilution with ID-CAMHB for cefiderocol and CAMHB for comparator agents
- MIC interpretations were performed for comparator antimicrobials using CLSI (2024) breakpoints (except for colistin where EUCAST criteria were used), while cefiderocol MIC results were interpreted as per CLSI, EUCAST and FDA criteria
- Carb-NS isolates were defined as those demonstrating a MIC value ≥4 mg/L (CLSI criteria) when challenged with imipenem and/or meropenem
  - Isolates meeting the criteria above were screened for the presence of MBL genes

Results[16]

- Of the 9572 *P. aeruginosa* isolates collected, 2236 (23.4%) were determined to be Carb-NS
  - Of these, 980/4400 (22.3%) originated from sites in the US and 1256/5172 (24.3%) originated from European sites
  - A total of 126/2236 (5.6%) carried MBL genes, and these isolates were mostly from European hospitals (94.4%)
- Against the overall population of Carb-NS *P. aeruginosa* isolates, cefiderocol had a MIC_{50} of 0.12 mg/L and a MIC_{90} of 0.5 mg/L (96–99.4% susceptible), including against both US and European isolate subsets – see Table 14
- Cefiderocol (85–96% susceptible) demonstrated activity against the MBL-carrying *P. aeruginosa* subset of isolates with a MIC_{50} value of 0.25 mg/L and a MIC_{90} of 2 mg/L – see Table 14
- All *P. aeruginosa* isolates determined to be carrying the MBL alleles bla_{IMP} and bla_{VIM} were susceptible to cefiderocol ($MIC_{90/100}$, 1/2 mg/L) according to the CLSI breakpoint – see Table 14
  - Higher cefiderocol MIC values ($MIC_{50/90}$, 2/16 mg/L) were obtained versus bla_{NDM}-carrying *P. aeruginosa* isolates

Table 14. *In Vitro* Activity of Cefiderocol and Comparator Antimicrobial Agents against Carbapenem-NS *P. aeruginosa* Isolates (and MBL-Carrying Subsets)[16]

Phenotype/Genotype[a] (n)	$MIC_{50/90}$ in mg/L (% S)[b]					
	Cefiderocol	Imipenem–relebactam	Ceftolozane–tazobactam	Ceftazidime–avibactam	Aztreonam–avibactam	Colistin
Carbapenem-NS (2236)	0.12/0.5 (99.2/98.6/96.3)	1/4 (85.5)	1/16 (85)	4/16 (85.3)	8/>16 (–)	0.5/1 (99.7)
US (980)	0.12/0.5 (99.4/98.9/96.6)	1/4 (89.5)	1/4 (90.2)	4/16 (86.9)	16/>16 (–)	0.5/1 (99.8)
Europe (1256)	0.12/0.5 (99/98.3/96)	1/>		4/32 (84)	8/>16 (–)	0.5/1 (99.7)
MBL-positive[c] (126)	0.25/2 (96/94.4/85)	>8		>32/>32 (4)	8/>16 (–)	0.5/1 (100)
bla_{IMP} (11)	0.5/1 (100/100/90.9)	>8/>		>32/>32 (0)	16/>16 (–)	0.5/1 (100)
bla_{NDM} (14)	2/16 (64.3/57.1/14.3)	>8/>8 (0)	>16/>16 (0)	>32/>32 (0)	4/>16 (–)	0.5/1 (100)
Bla_{VIM} (99)	0.12/1 (100/99/93.9)	>8/>8 (1)	>16/>16 (1)	32/>32 (5.1)	8/>16 (–)	0.5/1 (100)

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Surveillance Studies (Cont.)

Table 14. ***In Vitro*** **Activity of Cefiderocol and Comparator Antimicrobial Agents against Carbapenem-NS** ***P. aeruginosa*** **Isolates (and MBL-Carrying Subsets)**[16]

Phenotype/Genotype[a] (n)	$MIC_{50/90}$ in mg/L (% S)[b]					
	Cefiderocol	Imipenem–relebactam	Ceftolozane–tazobactam	Ceftazidime–avibactam	Aztreonam–avibactam	Colistin
Carbapenem-NS (2236)	0.12/0.5 (99.2/98.6/96.3)	1/4 (85.5)	1/16 (85)	4/16 (85.3)	8/>16 (–)	0.5/1 (99.7)
US (980)	0.12/0.5 (99.4/98.9/96.6)	1/4 (89.5)	1/4 (90.2)	4/16 (86.9)	16/>16 (–)	0.5/1 (99.8)
Europe (1256)	0.12/0.5 (99/98.3/96)	1/>8 (82.3)	1/>16 (80.9)	4/32 (84)	8/>16 (–)	0.5/1 (99.7)
MBL-positive[c] (126)	0.25/2 (96/94.4/85)	>8/>8 (2.4)	>16/>16 (0.8)	>32/>32 (4)	8/>16 (–)	0.5/1 (100)
bla_{IMP} (11)	0.5/1 (100/100/90.9)	>8/>8 (0)	>16/>16 (0)	>32/>32 (0)	16/>16 (–)	0.5/1 (100)
bla_{NDM} (14)	2/16 (64.3/57.1/14.3)	>8/>8 (0)	>16/>16 (0)	>32/>32 (0)	4/>16 (–)	0.5/1 (100)
bla_{VIM} (99)	0.12/1 (100/99/93.9)	>8/>8 (1)	>16/>16 (1)	32/>32 (5.1)	8/>16 (–)	0.5/1 (100)

Abbreviations: Carb-NS, carbapenem non-susceptible; CLSI, Clinical and Laboratory Standards Institute; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FDA, US Food and Drug Administration; MBL, metallo-β-lactamases; MIC, minimum inhibitory concentration; $MIC_{50/90}$, minimum inhibitory concentration to inhibit 50% and 90% of growth; NS, non-susceptible; S, susceptibility.

[a]Carb-NS isolates were those NS to imipenem and/or meropenem based on CLSI criteria (MIC values ≥4 mg/L).

[b]Cefiderocol MIC results were interpreted according to the CLSI/EUCAST/FDA criteria for susceptibility (≤4 mg/L, ≤2 mg/L, and ≤1 mg/L, respectively). MIC values for comparator agents were interpreted based on the CLSI criteria, except for colistin where the EUCAST susceptible breakpoint was applied.

[c]Includes the class B bla_{DIM-1} (2), bla_{IMP-1} (2), bla_{IMP-7} (4), bla_{IMP-8} (1), bla_{IMP-10} (1), bla_{IMP-13} (3), bla_{NDM-1} (14), bla_{VIM-1} (8), bla_{VIM-1} and bla_{HMB-1} (1), bla_{VIM-2} (80), bla_{VIM-4} (7), bla_{VIM-20} (2), and bla_{VIM-43} (1) genes.

Table adapted from Mendes et al. IDWeek. 2024.

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Surveillance Studies (Cont.)

DeJonge et al (2023) conducted an analysis on 299 DTR *P. aeruginosa* isolates collected from the SENTRY Antimicrobial Surveillance Program from the US and Europe (2020–2022).[17]

Methods[17]

- The *in vitro* activity of cefiderocol and comparator antibiotics was determined by broth microdilution according to CLSI methods using ID-CAHMB for cefiderocol and CAMHB for other antibiotics
- Susceptibility to cefiderocol was interpreted using FDA and CLSI (2023) breakpoints. The DTR phenotype was determined by being NS to β-lactam antibiotics and fluoroquinolones based on CLSI breakpoints

Results[17]

- Cefiderocol was active against 98.3% and 89.6% of *P. aeruginosa* isolates according to CLSI and FDA breakpoints, respectively – see **Table 15**

Table 15. Activity of Cefiderocol and Comparators against DTR[a] *P. aeruginosa* (N=299)[17]

Antimicrobial Agent	CLSI[b]			FDA[b]		
	%S	%I	%R	%S	%I	%R
Cefiderocol	98.3	1	0.7	89.6	8	2.3
Imipenem–relebactam	54.8	16.4	28.8	54.8	16.4	28.8
Meropenem–vaborbactam	–		–	–	–	–
Ceftazidime–avibactam	54.5		45.5	54.5	–	45.5
Ceftolozane–tazobactam	53.5		33.1	53.5	13.4	33.1
Piperacillin–tazobactam	3.7	11.7	84.6	3.7	11.7	84.6
Amikacin	[c]	72.6	27.4	62.9[c]	9.7	27.4
Colistin	–	99.7	0.3	–	–	–

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Surveillance Studies (Cont.)

Table 15. **Activity of Cefiderocol and Comparators against DTR[a] *P. aeruginosa* (N=299)**[17]

Antimicrobial Agent	CLSI[b]			FDA[b]		
	%S	%I	%R	%S	%I	%R
Cefiderocol	98.3	1	0.7	89.6	8	2.3
Imipenem–relebactam	54.8	16.4	28.8	54.8	16.4	28.8
Meropenem–vaborbactam	–	–	–	–	–	–
Ceftazidime–avibactam	54.5	–	45.5	54.5	–	45.5
Ceftolozane–tazobactam	53.5	13.4	33.1	53.5	13.4	33.1
Piperacillin–tazobactam	3.7	11.7	84.6	3.7	11.7	84.6
Amikacin	[c]	72.6	27.4	62.9[c]	9.7	27.4
Colistin	–	99.7	0.3	–	–	–

Abbreviations: CLSI, Clinical and Laboratory Standards Institute; DTR, difficult-to-treat resistant; FDA, US Food and Drug Administration; I, intermediate; NS, non-susceptible; R, resistant; S, susceptible.

[a]DTR *P. aeruginosa* was defined as being NS, based on CLSI breakpoints, to aztreonam, cefepime, ceftazidime, imipenem, meropenem, ciprofloxacin, and levofloxacin.

[b]Criteria as published by CLSI (2023) and FDA (2023).

[c]Using urinary tract infection only breakpoints.

Table adapted from DeJonge et al. IDWeek. 2023.

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Surveillance Studies (Cont.)

Shields et al (2023) evaluated the *in vitro* activity of cefiderocol against 178 *P. aeruginosa* isolates, of which 86 were NS to ceftazidime–avibactam, ceftolozane–tazobactam, and/or imipenem–relebactam.[18]

- Isolates included those from patients previously not treated with β-lactams (n=31), those with prior β-lactam exposure (n=69), and from isolates before and after treatment-emergent resistance to novel BL–BLIs (n=78)
- MICs were assessed via broth microdilution

Results[18]

- Of the 178 isolates collected, 177 harbored an OXA-50-like gene and all contained a chromosomal *ampC* gene
- The majority of isolates were either MDR (n=50) or XDR (n=102)
- Cefiderocol MICs were <2 mg/L in 94% of isolates, with a MIC_{50} and MIC_{90} of 0.06 mg/L and 0.25 mg/L, respectively
  - Against the ceftazidime–avibactam, ceftolozane–tazobactam, and imipenem–relebactam-NS isolates, the median cefiderocol MICs were 0.06, 0.03, and 0.06 mg/L, respectively
- Table 16 shows the comparison of cefiderocol MICs against isolates collected before and after treatment with BL–BLIs
- The cefiderocol MIC_{50} and MIC_{90} values were 0.25 mg/L and 4 mg/L, respectively, against isolates that were NS to ceftazidime–avibactam (n=59) or ceftolozane–tazobactam (n=58). In imipenem–relebactam-NS isolates (n=40), cefiderocol MIC_{50} was 0.25 mg/L and MIC_{90} was 2 mg/L
- The median MIC for cefiderocol doubled from 0.12 mg/L to 0.25 mg/L against isolates that were collected following exposure to any of these BL–BLIs (n=47) compared to baseline isolates that were from the same patients (n=31; *P*=0.1442)
- Overall, 14% (3/21) of isolates developed cefiderocol MIC >4 mg/L following exposure to ceftolozane–tazobactam

Table 16. Comparison of Cefiderocol MIC Values against Isolates Collected before and after Treatment with Ceftolozane–Tazobactam, Ceftazidime–Avibactam or Imipenem–Relebactam[18]

	Agent	Baseline MIC_{50} (mg/L)	Baseline MIC_{90} (mg/L)	Baseline MIC Range (mg/L)	Post-exposure MIC_{50} (mg/L)	Post-exposure MIC_{90} (mg/L)	Post-exposure MIC Range (mg/L)	*P* value[2]
		n=15			n=21			
Ceftolozane–tazobactam exposure	Ceftazidime–avibactam	4	16	1–32	64	256	4–256	<0.0001
	Ceftolozane–tazobactam	2	4	0.25–8	64	256	1–>64	<0.0001
	Cefiderocol	0.12	1	≤0.03–2	0.5	8	≤0.03–16	0.1034
	Imipenem–relebactam	2	8	≤0.06–8	2	4	0.25–32	0.6692
	Meropenem–vaborbactam	8	32		16	32	0.5–64	0.252
					n=9			
Ceftazidime–avibactam exposure	Ceftazidime–avibactam	4			16	64	4–128	0.0238
	Ceftolozane–tazobactam	2			4	16	2–16	0.0280
	Cefiderocol	0.06			0.06	0.25	≤0.03–0.25	>0.9999
	Imipenem–relebactam	1			1	4	0.12–8	0.4965
	Meropenem–vaborbactam	32	64		8	32	2–32	0.0909
		n=12			n=17			
Imipenem–relebactam exposure	Ceftazidime–avibactam	8	128	4–256	32	128	8–256	0.1986
	Ceftolozane–tazobactam	16	128	1–>64	8	64	1–>64	0.4307
	Cefiderocol	0.25	1	0.12–2	0.5	2	0.06–2	0.4038
	Imipenem–relebactam	1	2	0.25–2	4	16	2–32	<0.0001
	Meropenem–vaborbactam	8	16	2–32	16	64	8–64	0.0007

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Surveillance Studies (Cont.)

Table 16. Comparison of Cefiderocol MIC Values against Isolates Collected before and after Treatment with Ceftolozane–Tazobactam, Ceftazidime–Avibactam or Imipenem–Relebactam[18]

		Baseline			Post-exposure			
	Agent	**MIC_{50} (mg/L)**	**MIC_{90} (mg/L)**	**MIC Range (mg/L)**	**MIC_{50} (mg/L)**	**MIC_{90} (mg/L)**	**MIC Range (mg/L)**	***P* value[a]**
		n=15			n=21			
Ceftolozane–tazobactam exposure	Ceftazidime–avibactam	4	16	1–32	64	256	4–256	<0.0001
	Ceftolozane–tazobactam	2	4	0.25–8	64	256	1–>64	<0.0001
	Cefiderocol	0.12	1	≤0.03–2	0.5	8	≤0.03–16	0.1034
	Imipenem–relebactam	2	8	≤0.06–8	2	4	0.25–32	0.6692
	Meropenem–vaborbactam	8	32	1–32	16	32	0.5–64	0.252
		n=4			n=9			
Ceftazidime–avibactam exposure	Ceftazidime–avibactam	4	8	1–8	16	64	4–128	0.0238
	Ceftolozane–tazobactam	2	2	1–2	4	16	2–16	0.0280
	Cefiderocol	0.06	0.12	≤0.03–0.12	0.06	0.25	≤0.03–0.25	>0.9999
	Imipenem–relebactam	1	1	0.25–1	1	4	0.12–8	0.4965
	Meropenem–vaborbactam	32	64	8–64	8	32	2–32	0.0909
		n=12			n=17			
Imipenem–relebactam exposure	Ceftazidime–avibactam	8	128	4–256	32	128	8–256	0.1986
	Ceftolozane–tazobactam	16	128	1–>64	8	64	1–>64	0.4307
	Cefiderocol	0.25	1	0.12–2	0.5	2	0.06–2	0.4038
	Imipenem–relebactam	1	2	0.25–2	4	16	2–32	<0.0001
	Meropenem–vaborbactam	8	16	2–32	16	64	8–64	0.0007

Abbreviations: MIC, minimum inhibitory concentration; MIC_{50}, minimum inhibitory concentration at which 50% of isolates are inhibited; MIC_{90}, minimum inhibitory concentration at which 90% of isolates are inhibited.
[a]Comparison of non-rounded MIC_{50} by Mann-Whitney U test.
Table adapted from Shields et al. *JAC Antimicrob Resist*. 2023.

Fetroja® – Activity against Resistant *Pseudomonas aeruginosa*

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Relevant Prescribing Information

Fetroja® is indicated in patients 18 years of age or older for the treatment of:[23]

- 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:[23]

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

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Literature Search

As of February 2026, a computerized search of the published medical literature using internal and external databases (ie, PubMed®) has identified several additional relevant references regarding the activity of cefiderocol against resistant *P. aeruginosa*. For your review, these references are listed in the bibliography below:

- Xiao Y, Zhang J, Nie F, et al. Emergence of cefiderocol resistance mediated by bla_{AFM-1} overexpression and FptA mutations in clinical carbapenem-resistant *Pseudomonas aeruginosa* isolates. *Clin Microbiol Infect*. 2025:S1198-743X(25)00620-2. Online ahead of print. [Web Link]
- González-Pinto L, Gomis-Font AM, Pérez-Rodríguez G, et al. Contribution of mutational resistance mechanisms and acquired β-lactamases to cefiderocol/xeruborbactam susceptibility in *Pseudomonas aeruginosa*. *Antimicrob Agents Chemother*. 2025;69(12):e0104825. [Web Link]
- Loïez C, Charlet A, Duployez C, Le Guern R, Wallet F. β-lactamase inhibitors, cefiderocol and delafloxacin: evaluating promising antibiotics options for *Pseudomonas aeruginosa* in adults with cystic fibrosis. *New Microbiol*. 2025;48(3):234-237. [Web Link]
- Le Terrier C, Bouvier M, Kerbol A, et al. *In-vitro* activity of the novel β-lactam/β-lactamase inhibitor combinations and cefiderocol against carbapenem-resistant *Pseudomonas* spp. clinical isolates collected in Switzerland in 2022. *Eur J Clin Microbiol Infect Dis*. 2025;44(3):571-585. [Web Link]
- El Ghali A, Kunz Coyne AJ, Lucas K, et al. Cefiderocol: early clinical experience for multi-drug resistant Gram-negative infections. *Microbiol Spectr*. 2024;12(2):e0310823. [Web Link]
- Vacheron C-H, Kaas A, Rasigade J-P, et al. Cefiderocol in difficult-to-treat Nf-GNB in ICU settings (published correction appears in *Ann Intensive Care*. 2024;14(1):81. [Web Link]) *Ann Intensive Care*. 2024;14(1):73. [Web Link]
- Valzano F, La Bella G, Lopizzo T, et al. Resistance to ceftazidime-avibactam and other new β-lactams in *Pseudomonas aeruginosa* clinical isolates: a multi-center surveillance study. *Microbiol Spectr*. 2024;12(8):e0426623. [Web Link]
- Findlay J, Raro OHF, Poirel L, Nordmann P; NARA Network. Molecular analysis of metallo-beta-lactamase-producing *Pseudomonas aeruginosa* in Switzerland 2022-2023. *Eur J Clin Microbiol Infect Dis*. 2024;43(3):551-557. [Web Link]
- Gill CM, Santini D, Nicolau DP, ERACE-PA Global Study Group. *In vitro* activity of cefiderocol against a global collection of carbapenem-resistant *Pseudomonas aeruginosa* with a high level of carbapenemase diversity. *J Antimicrob Chemother*. 2024;79(2):412-416. [Web Link]
- Vega AD, DeRonde K, Jimenez A, et al. Difficult-to-treat (DTR) *Pseudomonas aeruginosa* harboring Verona-integron metallo-β-lactamase (bla_{VIM}): infection management and molecular analysis. *Antimicrob Agents Chemother*. 2024;68(5):e0147423. [Web Link]
- Abouelhassan Y, Gill CM, Nicolau DP. Assessing the *in vivo* efficacy of rational antibiotics and combinations against difficult-to-treat *Pseudomonas aeruginosa* producing GES β-lactamases. *J Antimicrob Chemother*. 2023;78(8):1843-1847. [Web Link]

Fetroja® – Activity against Resistant *Pseudomonas aeruginosa*

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Literature Search (Cont.)

- Brookfield C, Fadden E, Sweeney L. Successful use of prolonged cefiderocol monotherapy for the treatment of a complex pleural abscess caused by extensively drug-resistant (XDR) *Pseudomonas aeruginosa*. *JAC Antimicrob Resist*. 2023;5(5):dlad103. [Web Link]
- Malisova L, Vrbova I, Pomorska K, Jakubu V, Zemlickova H. *In vitro* activity of cefiderocol against carbapenem-resistant Enterobacterales and *Pseudomonas aeruginosa*. *Microb Drug Resist*. 2023;29(10):485-491. [Web Link]
- de la Fuente C, Rodríguez M, Merino N, et al. Real-life use of cefiderocol for salvage therapy of severe infections due to carbapenem-resistant Gram-negative bacteria. *Int J Antimicrob Agents*. 2023;62(1):106818. [Web Link]
- Tascini C, Antonelli A, Pini M, et al. Infective endocarditis associated with implantable cardiac device by metallo-β-lactamase-producing *Pseudomonas aeruginosa*, successfully treated with source control and cefiderocol plus imipenem. *Antimicrob Agents Chemother*. 2023;67(3):e0131322. [Web Link]
- Stevenson DR, Cherian BP, Kinzig M, Sörgel F, Wareham DW. Intravenous cefiderocol for neurosurgical meningitis from an extensively drug-resistant New-Delhi metallo- β-lactamase-producing *Pseudomonas aeruginosa* strain. *J Glob Antimicrob Resist*. 2023;32:29-30. [Web Link]
- Gras J, Villar-Fernandez S, Baylac P, et al. Successful cefiderocol therapy of severe infections due to difficult-to-treat *Pseudomonas aeruginosa* in two allogeneic hematopoietic stem cell transplantation recipients. *Ann Hematol*. 2022;101(6):1365-1367. [Web Link]
- Simner PJ, Cherian J, Suh GA, et al. Combination of phage therapy and cefiderocol to successfully treat *Pseudomonas aeruginosa* cranial osteomyelitis. *JAC Antimicrob Resist*. 2022;4(3):dlac046. [Web Link]
- Lasarte-Monterrubio C, Fraile-Ribot PA, Vázquez-Ucha JC, et al. Activity of cefiderocol, imipenem/ relebactam, cefepime/taniborbactam and cefepime/zidebactam against ceftolozane/tazobactam- and ceftazidime/avibactam-resistant *Pseudomonas aeruginosa*. *J Antimicrob Chemother*. 2022;77(10):2809-2815. [Web Link]
- Marcelo C, de Gea Grela A, Palazuelos MM, Veganzones J, Grandioso D, Díaz-Pollán B. Clinical cure of a difficult-to-treat resistant *Pseudomonas aeruginosa* ventriculitis using cefiderocol: a case report and literature review. *Open Forum Infect Dis*. 2022;9(8):ofac391. [Web Link]
- Borghesi L, Viaggi V, Franzetti M, et al. Successful prolonged cefiderocol treatment of a chronic left pleural empyema caused by *Pseudomonas aeruginosa* in a patient affected by COVID-19: a case report. *J Glob Antimicrob Resist*. 2021;27:157-159. [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]

Fetroja® – Activity against Resistant *Pseudomonas aeruginosa*

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Literature Search (Cont.)

- Streling AP, Al Obaidi MM, Lainhart WD, et al. Evolution of cefiderocol non-susceptibility in *Pseudomonas aeruginosa* in a patient without previous exposure to the antibiotic. *Clin Infect Dis*. 2021;73(11):e4472-e4474. [Web Link]
- Bodro M, Hernández-Meneses M, Ambrosioni J, et al. Salvage treatment with cefiderocol regimens in two intravascular foreign body infections by MDR Gram-negative pathogens, involving non-removable devices. *Infect Dis Ther*. 2021;10(1):575-581. [Web Link]
- Simner PJ, Beisken S, Bergman Y, Posch AE, Cosgrove SE, Tamma PD. Cefiderocol activity against clinical *Pseudomonas aeruginosa* isolates exhibiting ceftolozane-tazobactam resistance. *Open Forum Infect Dis*. 2021;8(7):ofab311. [Web Link]
- Cipko K, Gordon AK, Adhikari S, Konecny P. Cefiderocol treatment of *Pseudomonas aeruginosa* and extensively drug-resistant *Acinetobacter baumannii* retained spinal hardware infection causing reversible acute interstitial nephritis: Recto: Cefiderocol causing acute interstitial nephritis. *Int J Infect Dis*. 2021;109:108-111. [Web Link]
- Grasa CD, Gómez-Gil MR, San Román Pacheco S, et al. Compassionate use of cefiderocol for VIM metallo-β-lactamase-producing *Pseudomonas aeruginosa* infection in a toddler with Burkitt lymphoma. *J Glob Antimicrob Resist*. 2021;26:91-92. [Web Link]
- Roy AM, Hodgson M, Brickman C, MacDougall C. Cefiderocol as adjunctive treatment of necrotizing ventilator-associated pneumonia due to extensively drug-resistant *Pseudomonas aeruginosa*. *Infect Dis Clin Practice*. 2021;29(2):e111-e113. [Web Link]
- Bavaro DF, Romanelli F, Stolfa S, et al. Recurrent neurosurgical site infection by extensively drug-resistant *P. aeruginosa* treated with cefiderocol: a case report and literature review. *Infect Dis (Lond)*. 2021;53(3):206-211. [Web Link]
- Grande Perez C, Maillart E, Miendje Deyi VY, et al. Compassionate use of cefiderocol in a pancreatic abscess and emergence of resistance. *Infect Dis Now*. 2021;51(4):399-401. [Web Link]
- Kufel WD, Steele JM, Riddell SW, Jones Z, Shakeraneh P, Endy TP. Cefiderocol for treatment of an empyema due to extensively drug-resistant *Pseudomonas aeruginosa*: clinical observations and susceptibility testing considerations. *IDCases*. 2020;21:e00863. [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	ID-CAMHB	iron-depleted cation-adjusted Mueller Hinton broth
AE	adverse event	IH	in-hospital
ATM/AVI	aztreonam–avibactam	IMP	imipenemase
AUP	acute uncomplicated pyelonephritis	IQR	interquartile range
BAT	best available therapy	I/R	imipenem-relebactam
BJI	bone and joint infection	IV	intravenous
BL–BLI	β-lactam–β-lactamase inhibitor	KPC	*Klebsiella pneumoniae* carbapenemase
BSI	bloodstream infection	MBL	metallo-ß-lactamase
CAMHB	cation-adjusted Mueller Hinton broth	MDR	multidrug resistant
Carb-NS	carbapenem non-susceptible	MIC	minimum inhibitory concentration
CCI	Charlson Comorbidity Index	mITT	modified intent-to-treat
CFU	colony-forming unit	NA	not available/applicable
CI	confidence interval	ND	not detected
CLSI	Clinical and Laboratory Standards Institute	NDM	New Delhi metallo-β-lactamase
CNS	central nervous system	NS	non-susceptible
CR	carbapenem-resistant	OXA	oxacillinase
CRE	carbapenem-resistant Enterobacterales	PDC	*Pseudomonas*-derived cephalosporinase
CR-Micro-ITT	carbapenem-resistant microbiological intent-to-treat	PER	*Pseudomonas* extended resistance
cUTI	complicated urinary tract infection	PIP/TAZ	piperacillin–tazobactam
CZA	ceftazidime–avibactam	q8h	every 8 hours
DNA	deoxyribonucleic acid	q12h	every 12 hours
DTR	difficult-to-treat	R	resistant
EA	early assessment	RTI	respiratory tract infection
EOS	end of study	S	susceptible
EOT	end of treatment	SSSI	skin and skin structure infection
EUCAST	European Committee on Antimicrobial Susceptibility Testing	TOC	test of cure
FDA	US Food and Drug Administration	TOL/TAZ	ceftolozane–tazobactam
FU	follow-up	US	United States
g	grams	UTI	urinary tract infection
GES	Guiana extended-spectrum β-lactamase	VABP	ventilator-associated bacterial pneumonia
h	hours	VEB	Vietnamese extended-spectrum ß-lactamase
HABP	hospital-acquired bacterial pneumonia	VHA	Veterans Health Administration
HCABP	healthcare-associated bacterial pneumonia	VIM	Verona integron-mediated metallo-β-lactamase
I	intermediate	XDR	extensively drug resistant
IAI	intra-abdominal infection	%S	percent susceptible

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References

1. Portsmouth S, van Veenhuyzen D, Echols R, et al. Cefiderocol versus imipenem-cilastatin for the treatment of complicated urinary tract infections caused by Gram-negative uropathogens: a phase 2, randomised, double-blind, non-inferiority trial. *Lancet Infect Dis*. 2018;18(12):1319-1328. [Web Link]
2. Portsmouth S, van Veenhuyzen D, Echols R, et al. Cefiderocol versus imipenem-cilastatin for the treatment of complicated urinary tract infections caused by Gram-negative uropathogens: a phase 2, randomised, double-blind, non-inferiority trial (Supplementary Appendix). *Lancet Infect Dis*. 2018;18(12):1319-1328. [Web Link]
3. Wunderink RG, Matsunaga Y, Ariyasu M, et al. Cefiderocol versus high-dose, extended-infusion meropenem for the treatment of Gram-negative nosocomial pneumonia (APEKS-NP): a randomised, double-blind, phase 3, non-inferiority trial. *Lancet Infect Dis*. 2021;21(2):213-225. [Web Link]
4. Wunderink RG, Matsunaga Y, Ariyasu M, et al. Cefiderocol versus high-dose, extended-infusion meropenem for the treatment of Gram-negative nosocomial pneumonia (APEKS-NP): a randomised, double-blind, phase 3, non-inferiority trial (Supplementary Appendix). *Lancet Infect Dis*. 2021;21(2):213-225. [Web Link]
5. Data on File 24. Shionogi Inc.
6. Bassetti M, Echols R, Matsunaga Y, et al. Efficacy and safety of cefiderocol or best available therapy for the treatment of serious infections caused by carbapenem-resistant Gram-negative bacteria (CREDIBLE-CR): a randomised, open-label, multicentre, pathogen-focused, descriptive, phase 3 trial. *Lancet Infect Dis*. 2021;21(2):226-240. [Web Link]
7. Torre-Cisneros J, Almirante B, Martos CF, et al. Effectiveness and safety of cefiderocol treatment in patients with Gram-negative bacterial infections in Spain in the early access programme: results of the PERSEUS study. *Eur J Clin Microbiol Infect Dis*. 2025;44(6):1375-1390. [Web Link]
8. 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]
9. Clancy C, Cornely OA, Slover C, et al. Real-world effectiveness and safety of cefiderocol in the treatment of patients with serious Gram-negative bacterial infections: results of the PROVE chart review study. Poster presented at: IDWeek 2024; October 16-19, 2024; Los Angeles, CA.
10. Chou A, Ramsey D, Amenta E, Trautner BW. Real-world experience with cefiderocol therapy for *Pseudomonas aeruginosa* and other multidrug resistant Gram-negative infections within the Veterans Health Administration, 2019-2022. *Antimicrob Steward Healthc Epidemiol*. 2023;3(1):e90. [Web Link]
11. Satlin MJ, Simner PJ, Slover CM, Yamano Y, Nagata TD, Portsmouth S. Cefiderocol treatment for patients with multidrug- and carbapenem-resistant *Pseudomonas aeruginosa* infections in the compassionate use program. *Antimicrob Agents Chemother*. 2023;67(7):e0019423. [Web Link]
12. Kimbrough JH, Karr MH, Nguyen ST, et al. Activity of cefiderocol against *Pseudomonas aeruginosa* from the USA and Europe (2020-2023) with difficult-to-treat resistance phenotype, including those nonsusceptible to recently developed β-lactam/β-lactamase inhibitor combinations: results from the SENTRY antimicrobial surveillance program. *Microbiol Spectr*. 2025;13(11):e0207925. [Web Link]

Fetroja® – Activity against Resistant *Pseudomonas aeruginosa*

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References (Cont.)

13. Mendes RE, Maher JM, Kockler Z, Kimbrough JH, Castanheira M. *In vitro* activity of cefiderocol against resistant subsets of *Pseudomonas aeruginosa* collected from United States hospitals during 2020–2024. Poster presented at: IDWeek 2025; October 19-22, 2025; Atlanta, GA.
14. Yamano Y, DeJonge BLM, Nguyen ST, et al. Analyzing trends of cefiderocol susceptibility across five years of the SENTRY surveillance program. Poster presented at: IDWeek 2025; October 19-22, 2025; Atlanta, GA.
15. DeJonge BLM, Nguyen ST, Maher JM, et al. β-lactam–β-lactamase inhibitor combinations show a high degree of cross-resistance in Gram-negative bacteria, but not to cefiderocol. Data presented at: IDWeek 2025; October 19-22, 2025; Atlanta, GA.
16. Mendes RE, Beekman D, Karr M, Kimbrough JH, Sader HS, Castanheira M. Cefiderocol activity against *Pseudomonas aeruginosa* clinical isolates carrying metallo-β-lactamase genes in United States and European hospitals (2020–2023). Poster presented at: IDWeek 2024; October 16-19, 2024; Los Angeles, CA.
17. DeJonge BLM, Nguyen ST, Bryowsky JJ, et al. Activity of cefiderocol and comparator agents against difficult-to-treat resistant (DTR) Gram-negative isolates, collected during 2020–2022 as part of the SENTRY antimicrobial surveillance program. Poster presented at: IDWeek 2023; October 11-15, 2023; Boston, MA.
18. Shields RK, Kline EG, Squires KM, Van Tyne D, Doi Y. *In vitro* activity of cefiderocol against *Pseudomonas aeruginosa* demonstrating evolved resistance to novel β-lactam/β-lactamase inhibitors. *JAC Antimicrob Resist*. 2023;5(5):dlad107. [Web Link]
19. Data on File 4. Shionogi Inc.
20. Bassetti M, Echols R, Matsunaga Y, et al. Efficacy and safety of cefiderocol or best available therapy for the treatment of serious infections caused by carbapenem-resistant Gram-negative bacteria (CREDIBLE-CR): a randomised, open-label, multicentre, pathogen-focused, descriptive, phase 3 trial (Supplementary Appendix). *Lancet Infect Dis*. 2021;21(2):226-240. [Web Link]
21. Matsunaga Y, Ariyasu M, Takemura M, et al. Cefiderocol treatment for serious infections caused by carbapenem-resistant bacteria: post-hoc analysis of outcomes by pathogen in the CREDIBLE-CR study. Data presented at: IDWeek 2020; October 21-25, 2020; virtual congress.
22. Timsit JF, Paul M, Shields RK, et al. Cefiderocol for the treatment of infections due to metallo-β-lactamase-producing pathogens in the CREDIBLE-CR and APEKS-NP phase 3 randomized studies. *Clin Infect Dis*. 2022;75(6):1081-1084. [Web Link]
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Enclosure

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