Fetroja® – Cross-Resistance to Other Antibiotics

SHIONOGI

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Summary

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[1,2]
  - 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)
  - Overall, 210 (80.5%) patients achieved clinical cure at the end of treatment, and ACM at Day 28 occurred in 56 (21.5%) patients
    - Clinical cure was achieved in approximately 80% of infections that were resistant to meropenem, ceftolozane–tazobactam, ceftazidime–avibactam, or both ceftolozane–tazobactam and ceftazidime–avibactam
    - Day 28 ACM was approximately 20% in infections that were resistant to meropenem, ceftolozane–tazobactam, ceftazidime–avibactam, or both ceftolozane–tazobactam and ceftazidime–avibactam

PUBLISHED CASE REPORT

- **Bianco et al (2024)** described the case of a 64-year-old male patient with obesity and ESRD who underwent a combined heart–kidney transplantation. The patient experienced several bacterial infections in the ICU, leading to acute kidney injury requiring renal replacement therapy[3]
  - Treatment initiated on Day 120 for septic shock resulted in clinical improvement and the presence of a susceptible KPC-Kp isolate. Clinical improvement followed successful treatment of a new BSI caused by a KPC-Kp with ceftazidime–avibactam and cefiderocol susceptibility on Day 201. However, by Day 255, a KPC-Kp isolate was identified with cross-resistance to ceftazidime–avibactam, cefiderocol, and aztreonam–avibactam

IN VITRO STUDIES

- **Kimbrough et al (2025)** evaluated the activity of cefiderocol and various BL–BLI combinations against various subsets of *Pseudomonas 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[4]
  - 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.)

IN VITRO STUDIES (Cont.)

- **DeJonge et al (2024)** assessed the *in vitro* activity of cefiderocol against infections caused by Enterobacterales NS to BL–BLI combinations. In total, 24,084 Enterobacterales isolates were collected (from 33 hospitals in the US [n=11,884] and 39 hospitals across Europe and Israel [n=12,200]; with 1 [index] isolate per patient) as part of the SENTRY Antimicrobial Surveillance Program between 2020 and 2022[5]
  - When compared with the population overall, isolates that were NS to BL–BLI combinations had more elevated MIC values for cefiderocol
  - Cefiderocol retained activity (>84% using CLSI/FDA breakpoints) against Enterobacterales isolates that were NS to ceftazidime–avibactam, meropenem–vaborbactam, and imipenem–relebactam
  - There did not appear to be an identifiable common theme for the cross-resistance between cefiderocol and the various BL–BLI combinations, despite the high degree of such cross-resistance

- **Amadesi et al (2024)** described a retrospective analysis designed to investigate the development of resistance to cefiderocol in 6 patients (hospitalized in Bologna, Italy between 2017 and 2021) during treatment with ceftazidime–avibactam for infections caused by KPC-Kp[6]
  - Median ceftazidime–avibactam MICs increased after conclusion of therapy from 2 µg/mL (IQR, 2–8 µg/mL) to 256 µg/mL (IQR, 256–256 µg/mL)
  - In addition, there was an observed increase in cefiderocol MIC for all 6 patients, with a median value of 2 µg/mL (IQR, 1–2 µg/mL) rising to 16 µg/mL (IQR, 8–16 µg/mL)
  - WGS indicated that all strains collected prior to therapy harbored the KPC-3 variant, while 5 (83.3%) cefiderocol and ceftazidime–avibactam cross-resistant strains collected during therapy carried the KPC-31 variant (D179Y substitution), and 1 carried the KPC-130 variant (D179G substitution)

- **Santerre Henriksen et al (2024)** performed separate *in vitro* analyses of Enterobacterales, *P. aeruginosa*, and *Acinetobacter* spp. isolates collected from 6 European countries between January and December 2020. Susceptibility to cefiderocol and comparator agents were described using CLSI, FDA, and/or EUCAST breakpoints[7,8]
  - *In vitro* susceptibility testing of 1909 Enterobacterales, 950 *P. aeruginosa*, and 501 *Acinetobacter* spp. isolates showed that cefiderocol demonstrated high activity across species, with MIC_{90} values of 2, 1, and 2 mg/L, respectively, and susceptibility rates of 98.1%, 98.9%, and 92.4%
  - Cefiderocol retained high activity against almost all CR and comparator antibiotic-resistant isolates of Enterobacterales, *P. aeruginosa*, and *Acinetobacter* spp.

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Summary (Cont.)

IN VITRO 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. 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)[9]
  - Cefiderocol MICs were <2 mg/L in 94% of isolates, with a MIC_{50} and MIC_{90} of 0.06 and 0.25 mg/L, respectively
  - Cefiderocol MIC_{50} and MIC_{90} in the ceftolozane–tazobactam-NS (n=58) and ceftazidime–avibactam-NS (n=59) isolates was 0.25 and 4 mg/L, respectively. In imipenem–relebactam-NS (n=40) isolates, cefiderocol MIC_{50} was 0.25 mg/L and MIC_{90} was 2 mg/L
  - Overall, 3 (n=21; 14%) isolates developed a cefiderocol MIC >4 mg/L following exposure to ceftolozane–tazobactam

- **Poirel et al (2023)** evaluated the antimicrobial susceptibility of 2 previously identified KPC-3 variants of *Klebsiella pneumoniae* (KPC-41 and KPC-50) from clinical isolates that conferred high-level resistance to ceftazidime–avibactam[10]
  - Both variants were resistant to cefiderocol and ceftazidime–avibactam according to EUCAST breakpoints (>2 µg/mL and >8 µg/mL, respectively)
  - The MIC of cefiderocol against the recombinant strain containing KPC-50 was identical to that of the parent strain containing KPC-3, suggesting that an independent mutation in *K. pneumoniae* KPC-50 contributed to cefiderocol resistance

- **Werth et al (2022)** conducted a serial passage study of 3 independent *Stenotrophomonas maltophilia* strains in order to isolate cefiderocol-NS colonies that were then tested for susceptibility to cefiderocol and other antibiotic combinations to determine cross-resistance[11]
  - Isolates with reduced susceptibility to cefiderocol that were cross-resistant to ceftazidime–avibactam were observed
  - Although limited cross-resistance to other antibiotics was detected, a 4-fold decrease in trimethoprim–sulfamethoxazole MICs was observed in derivatives from 2 of the 3 strains (W357 and W364)

- **Lasarte-Monterrubio et al (2022)** evaluated 30 MDR/XDR *P. aeruginosa* strains resistant to ceftolozane–tazobactam and ceftazidime–avibactam due to various β-lactamases (variants of PDC, OXA-2, OXA-10), collected from multiple hospitals in Spain[12]
  - Many strains had MIC ranges of 8 to ≥512 mg/L for both ceftazidime–avibactam and ceftolozane–tazobactam
  - Cefiderocol was active against 29 of the 30 isolates, with a susceptibility rate of 96.6% (MIC range of ≤0.12 to 2 mg/L)

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Summary (Cont.)

IN VITRO STUDIES (Cont.)

- **Karlowsky et al (2022)** reported on the *in vitro* activity of cefiderocol against Gram-negative clinical isolates, including *P. aeruginosa*, *Acinetobacter baumannii*, Enterobacterales, and others, collected from North America and Europe in 5 multinational surveillance studies (SIDERO-WT-2014 to 2019)[13]
  - Cefiderocol demonstrated high *in vitro* activity (>90%) against all isolates, meropenem-NS isolates, ceftazidime–avibactam-NS isolates, and ceftolozane–tazobactam-NS isolates

- **Bianco et al (2022)** investigated the *in vitro* activity of cefiderocol against KPC-producing Enterobacterales (N=100), including clinical isolates susceptible or resistant to ceftazidime–avibactam, derived from a tertiary care teaching hospital in Italy[14]
  - Cefiderocol resistance was significantly higher in isolates resistant to ceftazidime–avibactam compared with those that were susceptible (P<0.001)
  - Cefiderocol $MIC_{50/90}$ values were 0.25 and 2 µg/mL, respectively, against ceftazidime–avibactam-susceptible isolates and 8 and 64 µg/mL, respectively, against ceftazidime–avibactam-resistant isolates

- **Simner et al (2021)** assessed the frequency of non-susceptibility to cefiderocol in a group of patients who were treated with ceftolozane–tazobactam for DTR *P. aeruginosa*. 16 paired isolates of DTR *P. aeruginosa* were obtained from patients before and after treatment with ceftolozane–tazobactam[15]
  - 10 of the 16 pairs of strains demonstrated increases in ceftolozane–tazobactam MICs (ranging from 8 to 256 µg/mL) after treatment with ceftolozane–tazobactam. Of the 10, only 1 strain demonstrated an increase in cefiderocol MIC (from 0.25 to 8 µg/mL)
  - 3 pairs of isolates developed ≥4-fold increases in MICs to cefiderocol after ceftolozane–tazobactam treatment, but remained susceptible to cefiderocol

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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.[1]

Methods[1]

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[1,2]

- 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)
- Cefiderocol was used as first-line treatment in 42 (16.1%) patients, the median treatment duration of cefiderocol treatment was 10 days, and cefiderocol was used in combination with other antibiotics in 91 (34.9%) patients, most commonly with colistin (19.5%)

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
- Clinical cure was achieved in approximately 80% of infections that were resistant to meropenem, or to ceftolozane–tazobactam, ceftazidime–avibactam, or both (see Table 1)
- Day 28 ACM was approximately 20% in infections that were resistant to meropenem, or to ceftolozane–tazobactam, ceftazidime–avibactam, or both (see Table 1)

Table 1. Clinical Outcomes by Previous Antibiotic Use and Resistance in the Overall Population[1,2]

Characteristic	Clinical Cure n (%)	Day 28 ACM n (%)	Composite Clinical Success n (%)
Meropenem-resistant (n=189)	152 (80.4)	39 (20.6)	160 (84.7)
Ceftolozane–tazobactam-resistant (n=99)	82 (82.8)	17 (17.2)	85 (85.9)
Ceftazidime–avibactam-resistant (n=134)	107 (79.9)	31 (23.1)	111 (82.8)
Cross-resistance to ceftolozane–tazobactam and ceftazidime–avibactam resistant (n=99)	[illegible]	17 (17.2)	85 (85.9)
Number of days with prior antibiotics (n=212) ≤3 (n=55) 4–7 (n=70) >7 (n=87)		9 (16.4) 13 (18.6) 25 (28.7)	49 (89.1) 62 (88.6) 67 (77)
Cefiderocol given as first-line treatment (n=42)		6 (14.3)	38 (90.5)
Cefiderocol administered as monotherapy (n=17[illegible])		30 (17.6)	150 (88.2)
Cefiderocol administered as combination (n=91)		26 (28.6)	70 (76.9)
Prior antibiotic treatment			
Ceftazidime–avibactam (n=81)	59 (72.8)	23 (28.4)	62 (76.5)
Ceftolozane–tazobactam (n=12)	9 (75)	2 (16.7)	10 (83.3)
Colistin (n=95)	74 (77.9)	25 (26.3)	78 (82.1)
Meropenem (n=80)	58 (72.5)	23 (28.8)	63 (78.8)

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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Real-World Evidence

Table 1. Clinical Outcomes by Previous Antibiotic Use and Resistance in the Overall Population[1,2]

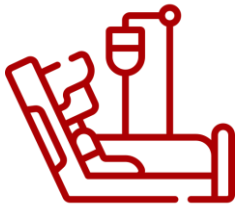
Characteristic	Clinical Cure n (%)	Day 28 ACM n (%)	Composite Clinical Success n (%)
Meropenem-resistant (n=189)	152 (80.4)	39 (20.6)	160 (84.7)
Ceftolozane–tazobactam-resistant (n=99)	82 (82.8)	17 (17.2)	85 (85.9)
Ceftazidime–avibactam-resistant (n=134)	107 (79.9)	31 (23.1)	111 (82.8)
Cross-resistance to ceftolozane–tazobactam and ceftazidime–avibactam (n=99)	82 (82.9)	17 (17.2)	85 (85.9)
Number of days with prior antibiotics (n=212) ≤3 (n=55) 4–7 (n=70) >7 (n=87)	 49 (89.1) 59 (84.3) 60 (69)	 9 (16.4) 13 (18.6) 25 (28.7)	 49 (89.1) 62 (88.6) 67 (77)
Cefiderocol given as first-line treatment (n=42)[a]	38 (90.5)	6 (14.3)	38 (90.5)
Cefiderocol administered as monotherapy (n=170)	143 (84.1)	30 (17.6)	150 (88.2)
Cefiderocol administered as combination (n=91)	67 (73.6)	26 (28.6)	70 (76.9)
Prior antibiotic treatment			
Ceftazidime–avibactam (n=81)	59 (72.8)	23 (28.4)	62 (76.5)
Ceftolozane–tazobactam (n=12)	9 (75)	2 (16.7)	10 (83.3)
Colistin (n=95)	74 (77.9)	25 (26.3)	78 (82.1)
Meropenem (n=80)	58 (72.5)	23 (28.8)	63 (78.8)

Abbreviation: ACM, all-cause mortality.
[a]Patients with first-line treatment received no prior antibiotic treatment for the current infection.
Table adapted from Torre-Cisneros et al. *Eur J Clin Microbiol Infect Dis*. 2025 (plus Supplementary Material).

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Published Case Report



Bianco et al (2024) described the case of a 64-year-old male patient with obesity (BMI, 33 kg/m^2) and ESRD who underwent a combined heart–kidney transplantation. During the post-operative period, rectal swabs revealed colonization with KPC-Kp and glycopeptide-resistant *Enterococcus faecium*. The patient experienced several bacterial infections in the ICU, leading to acute kidney injury requiring renal replacement therapy.[3]



- The patient was diagnosed with septic shock and empiric ceftazidime–avibactam 2.5 g q8h over 3 h plus IV fosfomycin 8 g q8h was initiated
- Blood cultures resulted in a susceptible KPC-Kp isolate and the patient improved after 7 days of treatment



- A new BSI with a ceftazidime–avibactam- and cefiderocol-susceptible KPC-Kp strain was identified
- Cefiderocol 2 g q8h over 3 h plus IV fosfomycin 8 g q8h was administered for a duration of 14 days, resulting in clinical improvement



- The patient presented with refractory septic shock due to a KPC-Kp isolate cross-resistant to ceftazidime–avibactam, cefiderocol, and aztreonam–avibactam
- The patient expired shortly thereafter

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In Vitro Studies

Kimbrough et al (2025) evaluated the 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.[4]

- 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[4]

- Overall, 98.6–99.8% (depending on breakpoint chosen) of *P. aeruginosa* isolates were shown to be susceptible to cefiderocol – see **Table 2**
  - 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 2**
  - 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 2**
  - 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 2. Activity of Cefiderocol and Comparator BL–BLI Combinations Tested against *P. aeruginosa* Isolates Collected from US and European Medical Centers (2020–2023)[4]

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		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		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

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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, nonsusceptible; 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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In Vitro Studies

Results (Cont.)[4]

- **Table 3** 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 4**
  - 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 3. 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)[4]

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
CZA	8	>32	1 to >32	52.3	47.7	52.3	47.7	52.3	47.7
I/R	2	>8	0.25 to >8	56	29.4	56	44	56	29.4
TOL/TAZ	4	>16	1 to >16	54.4	34.7	54.4	45.6	54.4	34.7
ATM/AVI	>16	>16	0.5 to >16						
PIP/TAZ	128	>128	32 to >128	0	88.9	*	100	0	100
Ceftazidime	>32	>32	16 to >32	0	86.7	*	100	0	100
Cefepime	32	>32	16 to >32	0	57.3	*	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	*	93.1	0	93.1
Aztreonam	>16	>16	16 to >16			*	81.4	0	81.4
Ciprofloxacin	>4	>4	1 to >4			85.1	*	100	0	85.1
Levofloxacin	16	>32	2 to >4			95.8	*	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			1	99.6	0.4	99	0.4
CZA	2	4	≤0.06 to >32			2.1	97.9	2.1	97.9	2.1
I/R	0.25	1	≤0.06 to >8			1.1	98.1	1.9	98.1	1.1
TOL/TAZ	0.5	2	≤0.12 to >16			1.5	97.6	2.4	97.6	1.5
ATM/AVI	4	16	≤0.03 to >16							
PIP/TAZ	4	64	≤0.06 to >128	82.6	11.7	*	17.4	72.4	17.4
Ceftazidime	2	16	0.06 to >32	86.4	9.9	*	13.6	86.4	13.6
Cefepime	2	16	0.06 to >32	89.4	3.2	*	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	*	14.4	81.6	14.4
Aztreonam	8	>16	0.06 to >16	75	15	*	15	75	15
Ciprofloxacin	0.12	2	≤0.008 to >4	84.1	11.2	*	15.9	84.1	11.2
Levofloxacin	0.5	4	≤0.015 to >32	75.5	14.7	*	14.7	75.5	14.7
Colistin	0.5	1	≤0.06 to >8		0.4	99.8	0.2		

Table 4. 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)[4]

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	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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In Vitro Studies

Table 3. 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)[4]

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
CZA	8	>32	1 to >32	52.3	47.7	52.3	47.7	52.3	47.7
I/R	2	>8	0.25 to >8	56	29.4	56	44	56	29.4
TOL/TAZ	4	>16	1 to >16	54.4	34.7	54.4	45.6	54.4	34.7
ATM/AVI	>16	>16	0.5 to >16						
PIP/TAZ	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
CZA	2	4	≤0.015 to >32	97.9	2.1	97.9	2.1	97.9	2.1
I/R	0.25	1	≤0.03 to >8	98.1	1.1	98.1	1.9	98.1	1.1
TOL/TAZ	0.5	2	≤0.12 to >16	97.6	1.5	97.6	2.4	97.6	1.5
ATM/AVI	4	16	≤0.03 to >16						
PIP/TAZ	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: ATM/AVI, aztreonam–avibactam; 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, nonsusceptible; PIP/TAZ, piperacillin–tazobactam; R, resistant; S, susceptible; TOL/TAZ, ceftolozane–tazobactam.

[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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In Vitro Studies

Table 4. 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)[4]

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, nonsusceptible; 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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In Vitro Studies (Cont.)

DeJonge et al (2024) assessed the *in vitro* activity of cefiderocol against infections caused by Enterobacterales NS to BL–BLI combinations. In total, 24,084 Enterobacterales isolates were collected between 2020 and 2022 as part of the SENTRY Antimicrobial Surveillance Program (from 33 hospitals in the US [n=11,884] and 39 hospitals across Europe and Israel [n=12,200]; with 1 [index] isolate per patient).[5]

- CLSI broth microdilution methodology was used to determine MIC values. ID-CAMHB was used for cefiderocol, while CAMHB was used for the various BL–BLI combinations. Antibiotic susceptibility was assessed according to 2024 CLSI, FDA, and EUCAST breakpoints. Non-susceptibility to the various BL–BLI combinations was assessed using CLSI breakpoints, and genetic analysis of cefiderocol-NS isolates was performed using WGS

Results[5]

- Overall, there was low resistance against the various BL–BLI combinations (≤1%), although resistance in Europe appeared to be higher (1–1.6%) compared with the US (0.2–0.3%)
- When compared with the population overall, isolates that were NS to BL–BLI combinations had more elevated MIC values for cefiderocol (**Figure 1**)
- Cefiderocol retained activity against Enterobacterales isolates that were NS to ceftazidime–avibactam (**Figure 2**)

Figure 1. MIC Distributions for Cefiderocol[5]

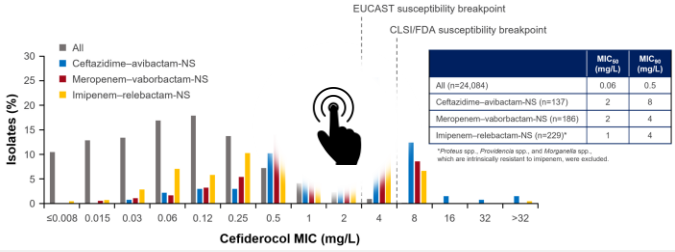
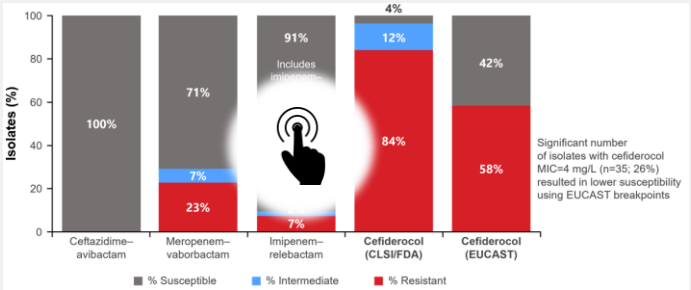


Figure 2. Susceptibility/Resistance Profile of Ceftazidime–Avibactam-NS Enterobacterales Isolates (n=137)[5]

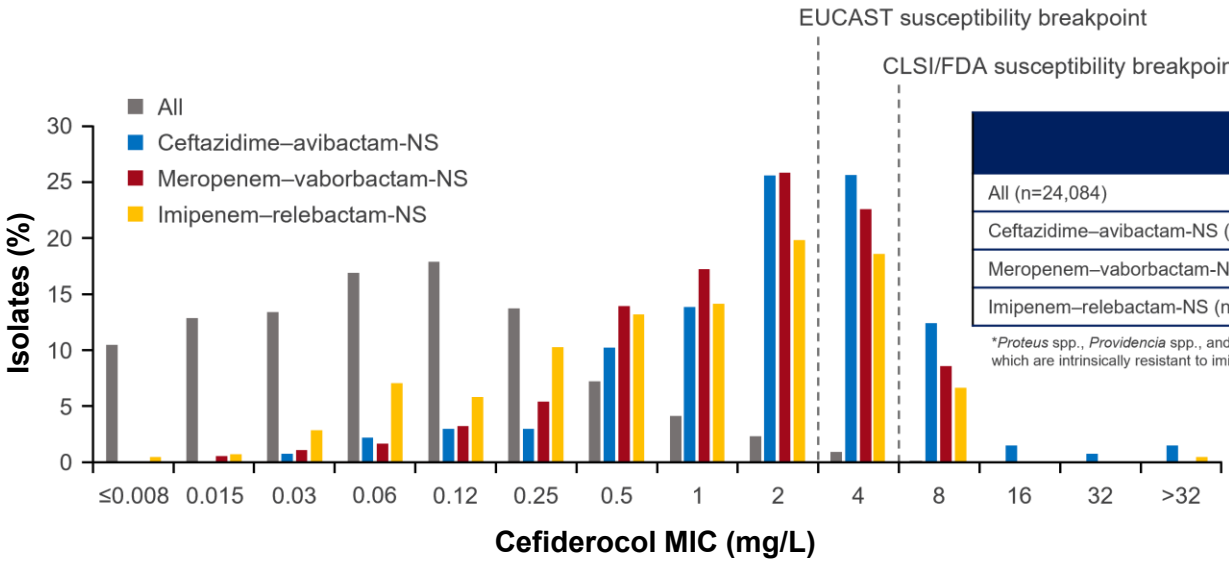


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In Vitro Studies (Cont.)

Figure 1. MIC Distributions for Cefiderocol[5]



	MIC_{50} (mg/L)	MIC_{90} (mg/L)
All (n=24,084)	0.06	0.5
Ceftazidime–avibactam-NS (n=137)	2	8
Meropenem–vaborbactam-NS (n=186)	2	4
Imipenem–relebactam-NS (n=229)*	1	4

**Proteus* spp., *Providencia* spp., and *Morganella* spp., which are intrinsically resistant to imipenem, were excluded.

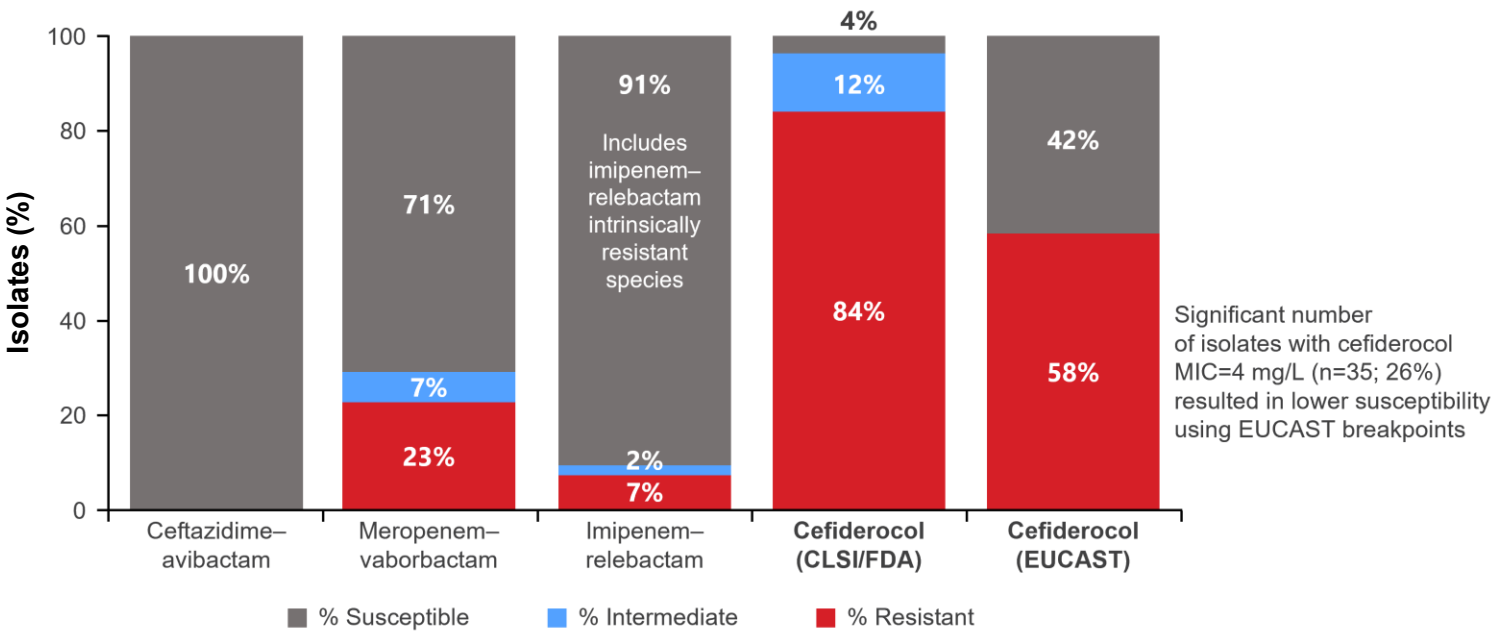
Abbreviations: CLSI, Clinical and Laboratory Standards Institute; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FDA, US Food and Drug Administration; MIC, minimum inhibitory concentration; MIC_{50}, minimum inhibitory concentration at which growth is inhibited in 50% of isolates; MIC_{90}, minimum inhibitory concentration at which growth is inhibited in 90% of isolates; NS, non-susceptible. Figure adapted from DeJonge et al. IDWeek 2024.

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In Vitro Studies (Cont.)

Figure 2. Susceptibility/Resistance Profile of Ceftazidime–Avibactam-NS Enterobacterales Isolates (n=137)[5,a]



Abbreviations: CLSI, Clinical and Laboratory Standards Institute; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FDA, US Food and Drug Administration; MBL, metallo-β-lactamase; MIC, minimum inhibitory concentration; NS, non-susceptible; OXA, oxacillinase.

[a]Characteristics: 0.57% of total isolates; Species distribution: *K. pneumoniae* 64%, *Enterobacter cloacae* species complex 17%, *Proteus mirabilis* 6%, *Escherichia coli* 4%; Species origin: Europe 87%, US 13%; β-lactamase content: MBL 79%, OXA-48-like + MBL 13%, other (including non-β-lactamase producers) 8%.

Figure adapted from DeJonge et al. IDWeek 2024.

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In Vitro Studies (Cont.)

Results (Cont.)[5]

- Cefiderocol retained activity against Enterobacterales isolates that were NS to meropenem–vaborbactam (**Figure 3**)
- Cefiderocol retained activity against Enterobacterales isolates that were NS to imipenem–relebactam (**Figure 4**)
- There did not appear to be an identifiable common theme for the cross-resistance between cefiderocol and the various BL–BLI combinations, despite the high degree of such cross-resistance
  - The only possible exception was 1 specific isolate (of 137) that was NS to ceftazidime–avibactam that contained KPC-31 (a KPC variant known to cause ceftazidime–avibactam and cefiderocol resistance) – **Table 5**
- Most cefiderocol-NS isolates had gene mutations known to play a role in reduced susceptibility to cefiderocol (including genes coding for iron transporters [*cir*, *fiu*], two-component regulation systems [*bae*, *envZ*], PBP-3 [*ftsI*], and/or efflux systems [*acr*A]), in addition to the presence of β-lactamases (mainly the MBLs)

Figure 3. Susceptibility/Resistance Profile of Meropenem–Vaborbactam-NS Enterobacterales Isolates (n=186)[5]

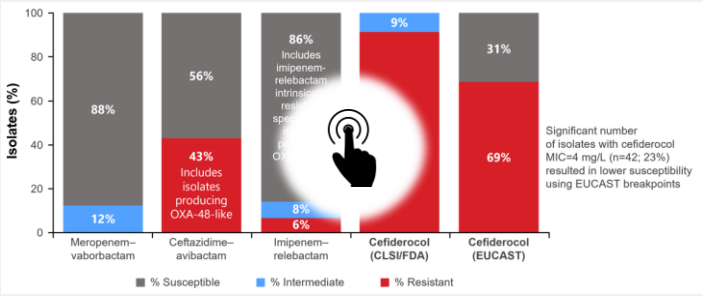


Figure 4. Susceptibility/Resistance Profile of Imipenem–Relebactam-NS Enterobacterales Isolates (n=229)[5]

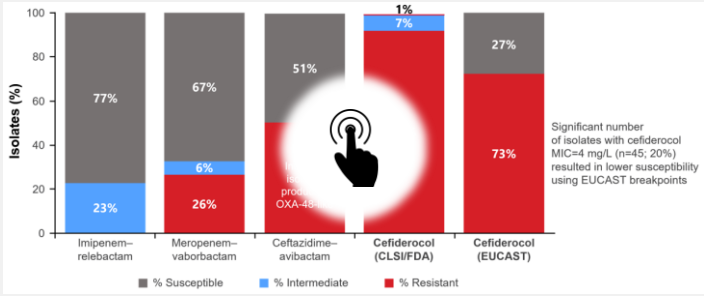


Table 5. Characteristics of Cefiderocol-NS Enterobacterales Isolates[5]

	Cefiderocol MIC (mg/L)		
	8	16	≥32
Ceftazidime–avibactam-NS	**13 MBL+**; 2 n 2 MB	**1 non-MBL+**; 1 non-MBL–	**1 non-MBL+**; 2 non-MBL– (1 PKC-31)
Meropenem–vaborbactam-NS	**13 MBL+**; 2 MB 1 MBL–		
Imipenem–relebactam-NS	**13 MBL+**; 2 MBL–; 1 MBL–		**1 non-MBL+**

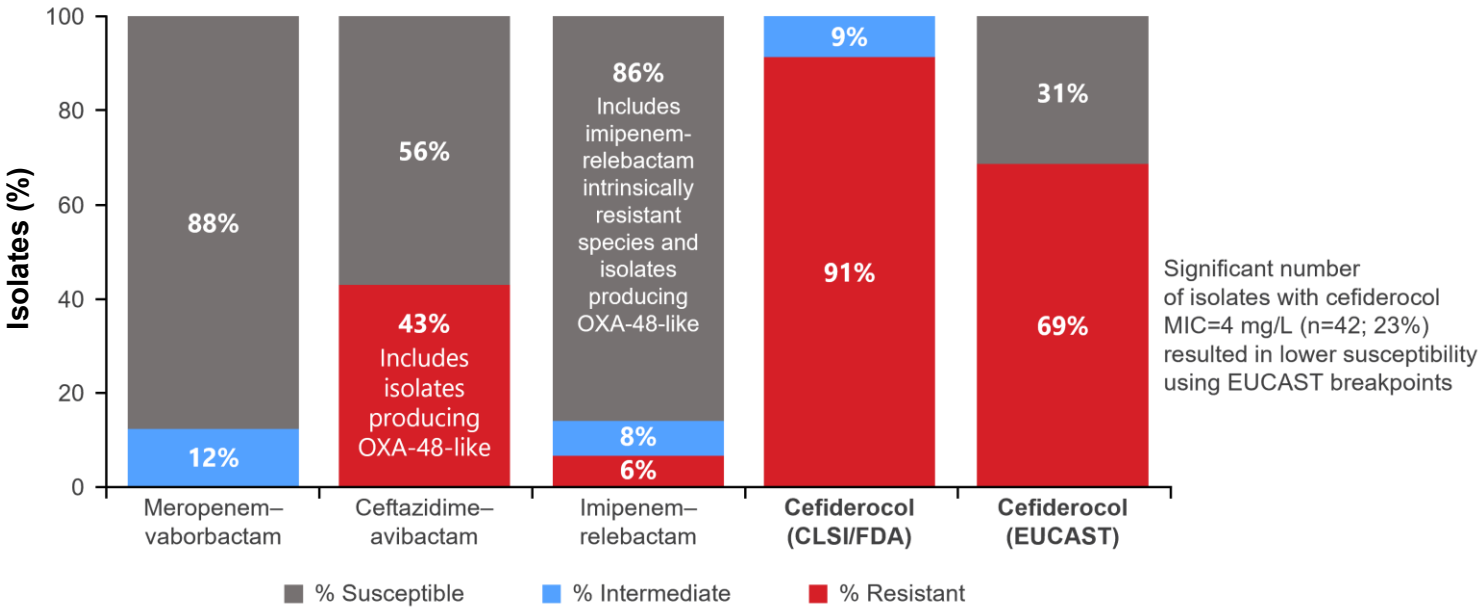
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In Vitro Studies (Cont.)

Figure 3. Susceptibility/Resistance Profile of Meropenem–Vaborbactam-NS Enterobacterales Isolates (n=186)[5,a]



Abbreviations: CLSI, Clinical and Laboratory Standards Institute; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FDA, US Food and Drug Administration; MBL, metallo-β-lactamase; MIC, minimum inhibitory concentration; NS, non-susceptible; OXA, oxacillinase.

[a]Characteristics: 0.77% of total isolates; Species distribution: *K. pneumoniae* 83%, *E. cloacae* species complex 9%, *E. coli* 4%; Species origin: Europe 89%, US 11%; β-lactamase content: MBL 45%, OXA-48-like + MBL 10%, OXA-48-like 34%, other (including non-β-lactamase producers) 11%.

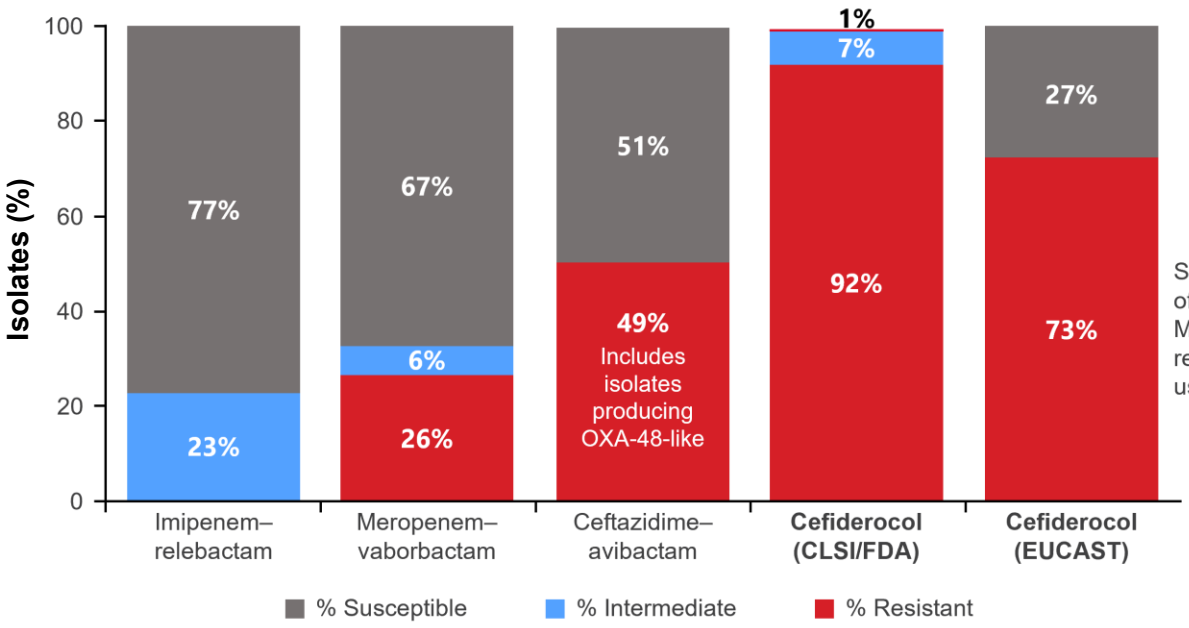
Figure adapted from DeJonge et al. IDWeek 2024.

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In Vitro Studies (Cont.)

Figure 4. Susceptibility/Resistance Profile of Imipenem–Relebactam-NS Enterobacterales Isolates (n=229)[5,a]



Significant number of isolates with cefiderocol MIC=4 mg/L (n=45; 20%) resulted in lower susceptibility using EUCAST breakpoints

Abbreviations: CLSI, Clinical and Laboratory Standards Institute; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FDA, US Food and Drug Administration; MBL, metallo-β-lactamase; MIC, minimum inhibitory concentration; NS, non-susceptible; OXA, oxacillinase.

[a]Characteristics: 1.05% of total isolates; Species distribution: *K. pneumoniae* 72%, *E. cloacae* species complex 9%, *Serratia marcescens* 7%; Species origin: Europe 86%, US 14%; β-lactamase content: MBL 41%, OXA-48-like + MBL 8%, OXA-48-like 34%, other (including non-β-lactamase producers) 17%.

Figure adapted from DeJonge et al. IDWeek 2024.

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In Vitro Studies (Cont.)

Table 5. Characteristics of Cefiderocol-NS Enterobacterales Isolates[5]

	Cefiderocol MIC (mg/L)		
	8	**16**	**≥32**
Ceftazidime–avibactam-NS	**13 MBL+**; **2 non-MBL+**; 2 MBL–	**1 non-MBL+**; 1 non-MBL–	**1 non-MBL+**; 2 non-MBL– (1 PKC-31)
Meropenem–vaborbactam-NS	**13 MBL+**; 2 MBL–; 1 MBL–		
Imipenem–relebactam-NS	**13 MBL+**; 2 MBL–; 1 MBL–		**1 non-MBL+**

+: isolates with additional gene mutations implicated in reduced cefiderocol susceptibility;
–: isolates with no additional gene mutations implicated in reduced cefiderocol susceptibility.
Abbreviations: KPC, *K. pneumoniae* carbapenemase; MBL, metallo-β-lactamase; MIC, minimum inhibitory concentration; NS, non-susceptible.
Table adapted from DeJonge et al. IDWeek 2024.

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In Vitro Studies (Cont.)

Amadesi et al (2024) described a retrospective analysis designed to investigate the development of resistance to cefiderocol in 6 patients (hospitalized in Bologna, Italy between 2017 and 2021) during treatment with ceftazidime–avibactam for infections caused by KPC-Kp. Samples were collected using rectal swabs or via the blood. Antibiotic susceptibility testing was performed using an automated system, except for cefiderocol which was achieved by broth microdilution using ID-CAMHB, and MIC values were evaluated according to EUCAST breakpoints. Genetic analysis of isolates was accomplished using WGS.[6]

Results[6]

- All 6 patients received ceftazidime–avibactam-based therapy for a median of 25 days, and subsequently developed resistance within a median of 23 days following antibiotic exposure
- Median ceftazidime–avibactam MICs increased after conclusion of therapy from 2 µg/mL (IQR, 2–8 µg/mL) to 256 µg/mL (IQR, 256–256 µg/mL)
- In addition, there was an observed increase in cefiderocol MIC for all 6 patients, with a median value of 2 µg/mL (IQR, 1–2 µg/mL) rising up to 16 µg/mL (IQR, 8–16 µg/mL) – see **Table 6**
- Analyses using WGS indicated that all strains collected prior to therapy harbored the KPC-3 variant, while 5 (83.3%) cefiderocol and ceftazidime–avibactam cross-resistant strains collected during therapy carried the KPC-31 variant (D179Y substitution), and 1 carried the KPC-130 variant (D179G substitution) – see **Table 6**

Table 6. Genetics and Antibiotic Susceptibility of the KPC-Kp Isolates[6]

Patient	Days of Exposure to CZA (Prior to RE)	Isolate Name	Isolation Source	MIC (µg/mL)					Carbapenemase Gene Mutation
				CZA	MER	MER/VAB	I/R	Cefiderocol	
1	17 (17)	BOT-CA-S	Blood	8 (S)	**256 (R)**	**32 (R)**	2 (S)	1 (S)	bla_{KPC-3}
		BOT-EMO	Blood	**>256 (R)**	**256 (R)**	8 (S)	1 (S)	**16 (R)**	bla_{KPC-31} (D179Y)
2	58 (42)	CAZ26	Rectal swab	2 (S)	**256 (R)**	2 (S)	1 (S)	1 (S)	bla_{KPC-3}
		CAZ30	Rectal swab	>25		0.064 (S)	0.25 (S)	**16 (R)**	bla_{KPC-31} (D179Y)
3	9 (7)	CAZ83	Rectal swab			0.064 (S)	0.032 (S)	2 (S)	bla_{KPC-3}
		CAZ85	Blood	2		0.064 (S)	0.032 (S)	**8 (R)**	bla_{KPC-31} (D179Y)
4	32 (29)	BAT68	Rectal swab	4		0.5 (S)	1 (S)	2 (S)	bla_{KPC-3}
		CAZ90	Rectal swab	**>256 (R)**	**256 (R)**	4 (S)	0.25 (S)	**8 (R)**	$bla_{KPC-130}$ (D179G)
5	31 (28)	CAZ89	Rectal swab	2 (S)	8 (S)	0.032 (S)	0.25 (S)	2 (S)	bla_{KPC-3}
		CAZ107	Blood	**>256 (R)**	**256 (R)**	0.032 (S)	0.25 (S)	**16 (R)**	bla_{KPC-31} (D179Y)
6	19 (9)	CAZ112	Rectal swab	2 (S)	**256 (R)**	1 (S)	0.5 (S)	**4 (R)**	bla_{KPC-3}
		CAZ147	Blood	**256 (R)**	2 (S)	2 (S)	1 (S)	**16 (R)**	bla_{KPC-31} (D179Y)

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In Vitro Studies (Cont.)

Table 6. Genetics and Antibiotic Susceptibility of the KPC-Kp Isolates[6]

Patient	Days of Exposure to CZA (Prior to RE)	Isolate Name	Isolation Source	MIC (µg/mL)					Carbapenemase Gene Mutation
				CZA	MER	MER/VAB	I/R	Cefiderocol	
1	17 (17)	BOT-CA-S	Blood	8 (S)	**256 (R)**	**32 (R)**	2 (S)	1 (S)	bla_{KPC-3}
		BOT-EMO	Blood	**>256 (R)**	**256 (R)**	8 (S)	1 (S)	**16 (R)**	bla_{KPC-31} (D179Y)
2	58 (42)	CAZ26	Rectal swab	2 (S)	**256 (R)**	2 (S)	1 (S)	1 (S)	bla_{KPC-3}
		CAZ30	Rectal swab	**>256 (R)**	**256 (R)**	0.064 (S)	0.25 (S)	**16 (R)**	bla_{KPC-31} (D179Y)
3	9 (7)	CAZ83	Rectal swab	2 (S)	8 (S)	0.064 (S)	0.032 (S)	2 (S)	bla_{KPC-3}
		CAZ85	Blood	**>256 (R)**	≤0.1 (S)	0.064 (S)	0.032 (S)	**8 (R)**	bla_{KPC-31} (D179Y)
4	32 (29)	BAT68	Rectal swab	4 (S)	**256 (R)**	0.5 (S)	1 (S)	2 (S)	bla_{KPC-3}
		CAZ90	Rectal swab	**>256 (R)**	**256 (R)**	4 (S)	0.25 (S)	**8 (R)**	$bla_{KPC-130}$ (D179G)
5	31 (28)	CAZ89	Rectal swab	2 (S)	8 (S)	0.032 (S)	0.25 (S)	2 (S)	bla_{KPC-3}
		CAZ107	Blood	**>256 (R)**	**256 (R)**	0.032 (S)	0.25 (S)	**16 (R)**	bla_{KPC-31} (D179Y)
6	19 (9)	CAZ112	Rectal swab	2 (S)	**256 (R)**	1 (S)	0.5 (S)	**4 (R)**	bla_{KPC-3}
		CAZ147	Blood	**256 (R)**	2 (S)	2 (S)	1 (S)	**16 (R)**	bla_{KPC-31} (D179Y)

Resistance is indicated in bold text.
Abbreviations: CZA, ceftazidime–avibactam; I/R, imipenem–relebactam; KPC, *K. pneumoniae* carbapenemase; MER/VAB, meropenem–vaborbactam; MIC, minimum inhibitory concentration; R, resistant; RE, resistance emergence; S, susceptible.
Table adapted from Amadesi et al. *Diagn Microbiol Infect Dis*. 2024.

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In Vitro Studies (Cont.)

Santerre Henriksen et al (2024) performed 2 separate *in vitro* analyses of cefiderocol and comparator agents against Enterobacterales, *P. aeruginosa*, and *Acinetobacter* spp. isolates collected in 6 European countries in 2020.[7,8]

Enterobacterales[7]

- Overall, 1909 Enterobacterales isolates were collected
  - The most common pathogens were *Klebsiella* spp. (n=970), *E. coli* (n=382), and *Enterobacter* spp. (n=244)
  - The most common infections sites were bloodstream (43.6%), respiratory tract (22.6%), and skin (16.0%)
  - Of the 1909 isolates collected, 148 (7.8%) were CRE, with various β-lactamases identified, including MBLs
- Cefiderocol demonstrated strong activity against the Enterobacterales isolates and remained highly active against almost all of the CR + comparator antibiotic-resistant isolates (Table 7)

P. aeruginosa and *Acinetobacter* spp.[8]

- Overall, 1451 isolates were collected (950 [65.5%] *P. aeruginosa* and 501 [34.5%] *Acinetobacter* spp.)
  - The most common infection sites for both pathogens were respiratory tract, bloodstream, and skin
  - In total, 139/950 (14.6%) of the *P. aeruginosa* isolates and 227/501 (45.3%) of the *Acinetobacter* spp. isolates, were CR
  - Cefiderocol susceptibility rates were determined used CLSI or FDA breakpoints, depending on availability
- Susceptibility rates of cefiderocol were high against *P. aeruginosa* isolates (Table 8)
  - Cefiderocol retained activity against almost all of the CR + comparator antibiotic-resistant isolates of both *P. aeruginosa* and *Acinetobacter* spp.

Table 7. *In Vitro* Activity of Cefiderocol, Other Antibiotics, and Antibiotic Combinations Tested against Enterobacterales Isolates with Resistant Phenotypes[7]

Isolate (n)	Cefiderocol		MEM		CZA		C/T		MVB		I/R		ATM/AVI		FEP/TAN		(CST)	
	MIC_{50} (mg/L)	S (%)	MIC_{50} (mg/L)	S (%)	MIC_{50} (mg/L)	S (%)	MIC_{50} (mg/L)	S (%)	MIC_{50} (mg/L)	S (%)	MIC_{50} (mg/L)	S (%)	MIC_{50} (mg/L)	S (%)	MIC_{50} (mg/L)	S (%)	MIC_{50} (mg/L)	S (%)
All Enterobacterales[a] (1909)	2	98.1	4	92.2	1	95	>32	78.1	0.5	97.4	1	94.7	≤1	99.1	0.5	98.7	(>8)	(95.3)
Cefiderocol-R (37)	—	—	>16	51.4	>16	35.1	>32	10.8	>32	56.8	>16	35.1	≤1	94.6	16	78.4	(>8)	(83.3)
MEM-R (148)	4	87.8	—	—	>16	71.6	>32	0	>32	70.9	>16	69.9	≤1	98.6	4	93.2	(1)	(91.1)
CZA-R (86)	8	75	>16	56.3	—	—	>32	11.5	>32	62.5	>16	31.9	≤1	97.9	8	89.6	(1)	(92.6)
C/T-R (419)	2	92.1	>16	64.7	>16	79.7	—	—	16	88.1	8	77.7	≤1	96.7	4	95.2	(1)	(92.8)
MVB-R (50)	8	68	>16	14	>16	28	>32	0	—	—	>16	4.3	>32	86	16	68	(1)	(91.5)
I/R-R (95)	8	74.7	>16	53.7	>16	32.6	[illegible]		[illegible]		52.6	—	4	90.5	16	84.2	(1)	(92.3)
FEP/TAN-R (24)	8	66.7	>16	58.3	>16	58.3	[illegible]		[illegible]		33.3	>16	31.8	>32	66.7	—	(1)	(96)
CST-R (79)	2	92.4	>16	83.5	2	[illegible]	[illegible]		[illegible]		1	2	91.1	≤1	100	2	97.5	—
MEM-R & CZA-R (82)	8	61.9	—	—	—	[illegible]	[illegible]		[illegible]		[illegible]	>16	11.9	1	97.6	16	76.2	(8)	(85.7)
MEM-R & MVB-R (43)	8	65.1	—	—	>16	[illegible]	[illegible]		[illegible]		[illegible]	>16	4.7	1	97.7	16	76.7	(8)	(86)
MEM-R & I/R-R (44)	8	65.9	—	—	>16	[illegible]	[illegible]		[illegible]		[illegible]	—	—	≤1	95.5	16	79.5	(1)	(90.9)
Klebsiella spp. (970)	2	98.7	>16	86.9	2	[illegible]	[illegible]		[illegible]		1	94.7	≤1	99.1	1	99	(≤0.25)	(96.3)
MEM-R (127)	2	95.3	—	—	>16	[illegible]	[illegible]		[illegible]		16	79.5	≤1	98.4	4	97.6	(0.5)	(92.9)
CZA-R (42)	4	83.3	>16	45.2	—	[illegible]	[illegible]		[illegible]		>16	35.7	≤1	95.2	4	92.9	(1)	(92.9)
C/T-R (270)	2	96.3	>16	53	>16	85.6	[illegible]		[illegible]		89.6	8	81.9	≤1	96.7	2	96.7	(0.5)	(94.4)
MVB-R (28)	4	85.7	>16	17.9	>16	39.3	>32	0	—	—	>16	7.1	>32	82.1	>32	75	(0.5)	(96.4)
I/R-R (51)	4	88.2	>16	49	>16	47.1	>32	3.9	>32	49	—	—	32	84.3	8	86.3	(1)	(92.2)
CST-R (36)	2	100	>16	75	2	91.7	>32	58.3	1	97.2	4	88.9	≤1	100	2	100	—	—
E. coli (382)	1	99.2	≤0.25	99.5	≤0.25	96.9	1	93.7	≤0.06	99.5	0.25	98.7	≤1	99.2	≤0.25	99.2	(≤0.25)	(98.7)
C/T-R (24)	4	87.5	8	91.7	>16	79.2	—	—	4	91.7	8	79.2	≤1	91.7	4	95.8	(≤0.25)	(100)
Enterobacter spp. (244)	2	92.2	4	93.9	>16	84.8	>32	61.1	2	93.9	4	86.5	≤1	99.6	0.5	97.5	(>8)	(86.9)
CZA-R (37)	16	59.5	>16	64.9	—	—	>32	0	>32	64.9	>16	16.2	≤1	100	8	86.5	(1)	(91.9)
C/T-R (95)	8	81.1	>16	84.2	>16	61.1	—	—	32	84.2	16	65.3	≤1	98.9	2	93.7	(>8)	(85.3)
I/R-R (33)	16	54.5	>16	57.6	>16	6.1	>32	0	>32	54.5	—	—	≤1	97	16	81.8	(1)	(90.9)
CST-R (32)	4	81.3	>16	87.5	1	90.6	>32	56.3	0.5	90.6	2	90.6	≤1	100	2	93.8	—	—

Table 8. *In Vitro* Activity of Cefiderocol, Other Antibiotics, and Antibiotic Combinations Tested against *P. aeruginosa* and *Acinetobacter* spp. Isolates with Resistant Phenotypes[8]

Isolate (n)	Susceptibility[a] (%)									
	Cefiderocol	MEM	CZA	C/T	MVB	I/R	ATM/AVI	FEP/TAN	SUL/DUR	(CST)
P. aeruginosa (950)	98.9	85.4	90.1	89.1	87.2	83.3	86.2	91.4	NA	(99.7)
MEM-R (139)	97.8	—	56.8	55.4	12.2	12.2	41.7	59.7	NA	(100)
CZA-R (94)	93.6	36.2	—	[illegible]	39.4	37.2	54.3	55.3	NA	(100)
C/T-R (104)	94.2	40.4	[illegible]			36.5	64.4	59.6	NA	(100)
MVB-R (122)	97.5	0	[illegible]			10.7	38.5	59	NA	(100)
I/R-R (159)	98.1	23.3	[illegible]			—	54.1	64.8	NA	(100)
ATM/AVI-R (131)	95.4	38.2	[illegible]			44.3	—	61.8	NA	(100)
FEP/TAN-R (82)	95.1	31.7	48			31.7	39	—	NA	(100)
MEM-R & CZA-R (60)	96.7	—	—	[illegible]	5	8.3	45	43.3	NA	(100)
MEM-R & C/T-R (62)	98.4	—	30.6	—	8.1	9.7	54.8	50	NA	(100)
Acinetobacter spp. (501)[b]	92.4	54.7	NA	NA	NA	NA	NA	NA	97	(98.4)
Cefiderocol-R (38)	—	10.5	NA	NA	NA	NA	NA	NA	65.8	(92.1)
MEM-R (227)	85	—	NA	NA	NA	NA	NA	NA	93.8	(97.4)
SUL/DUR-R[c] (15)	13.3	6.7	NA	NA	NA	NA	NA	NA	—	(100)

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In Vitro Studies (Cont.)

Table 7. *In Vitro* Activity of Cefiderocol, Other Antibiotics, and Antibiotic Combinations Tested against Enterobacterales Isolates with Resistant Phenotypes[7]

Isolate (n)	Cefiderocol		MEM		CZA		C/T		MVB		I/R		ATM/AVI		FEP/TAN		(CST)	
	MIC_{90} (mg/L)	S (%)	MIC_{90} (mg/L)	S (%)	MIC_{90} (mg/L)	S (%)	MIC_{90} (mg/L)	S (%)	MIC_{90} (mg/L)	S (%)	MIC_{90} (mg/L)	S (%)	MIC_{90} (mg/L)	S (%)	MIC_{90} (mg/L)	S (%)	MIC_{90} (mg/L)	S (%)
All Enterobacterales[a] (1909)	2	98.1	4	92.2	1	95	>32	78.1	0.5	97.4	1	94.7	≤1	99.1	0.5	98.7	(>8)	(95.3)
Cefiderocol-R (37)	—	—	>16	51.4	>16	35.1	>32	10.8	>32	56.8	>16	35.1	≤1	94.6	16	78.4	(>8)	(83.3)
MEM-R (148)	4	87.8	—	—	>16	71.6	>32	0	>32	70.9	>16	69.9	≤1	98.6	4	93.2	(1)	(91.1)
CZA-R (96)	8	75	>16	56.3	—	—	>32	11.5	>32	62.5	>16	31.9	≤1	97.9	8	89.6	(1)	(92.6)
C/T-R (419)	2	92.1	>16	64.7	>16	79.7	—	—	16	88.1	8	77.7	≤1	96.7	4	95.2	(1)	(92.8)
MVB-R (50)	8	68	>16	14	>16	28	>32	0	—	—	>16	4.3	>32	86	16	68	(1)	(91.5)
I/R-R (95)	8	74.7	>16	53.7	>16	32.6	>32	4.2	>32	52.6	—	—	4	90.5	16	84.2	(1)	(92.3)
FEP/TAN-R (24)	8	66.7	>16	58.3	>16	58.3	>32	16.7	>32	33.3	>16	31.8	>32	66.7	—	—	(1)	(90)
CST-R (79)	2	92.4	>16	83.5	2	91.1	>32	63.3	1	94.9	2	91.1	≤1	100	2	97.5	—	—
MEM-R & CZA-R (42)	8	61.9	—	—	—	—	>32	0	>32	16.7	>16	11.9	1	97.6	16	76.2	(8)	(85.7)
MEM-R & MVB-R (43)	8	65.1	—	—	>16	18.6	>32	0	—	—	>16	4.7	1	97.7	16	76.7	(8)	(86)
MEM-R & I/R-R (44)	8	65.9	—	—	>16	20.5	>32	0	>32	11.4	—	—	≤1	95.5	16	79.5	(1)	(90.9)
Klebsiella spp. (970)	2	98.7	>16	86.9	2	95.7	>32	72.2	1	97.1	1	94.7	≤1	99.1	1	99	(≤0.25)	(96.3)
MEM-R (127)	2	95.3	—	—	>16	81.9	>32	0	32	81.9	16	79.5	≤1	98.4	4	97.6	(0.5)	(92.9)
CZA-R (42)	4	83.3	>16	45.2	—	—	32	7.1	>32	59.5	>16	35.7	≤1	95.2	4	92.9	(1)	(92.9)
C/T-R (270)	2	96.3	>16	53	>16	85.6	—	—	16	89.6	8	81.9	≤1	96.7	2	96.7	(0.5)	(94.4)
MVB-R (28)	4	85.7	>16	17.9	>16	39.3	>32	0	—	—	>16	7.1	>32	82.1	>32	75	(0.5)	(96.4)
I/R-R (51)	4	88.2	>16	49	>16	47.1	>32	3.9	>32	49	—	—	32	84.3	8	86.3	(1)	(92.2)
CST-R (36)	2	100	>16	75	2	91.7	>32	58.3	1	97.2	4	88.9	≤1	100	2	100	—	—
E. coli (382)	1	99.2	≤0.25	99.5	≤0.25	96.9	1	93.7	≤0.06	99.5	0.25	98.7	≤1	99.2	≤0.25	99.2	(≤0.25)	(98.7)
C/T-R (24)	4	87.5	8	91.7	>16	79.2	—	—	4	91.7	8	79.2	≤1	91.7	4	95.8	(≤0.25)	(100)
Enterobacter spp. (244)	2	92.2	4	93.9	>16	84.8	>32	61.1	2	93.9	4	86.5	≤1	99.6	0.5	97.5	(>8)	(86.9)
CZA-R (37)	16	59.5	>16	64.9	—	—	>32	0	>32	64.9	>16	16.2	≤1	100	8	86.5	(1)	(91.9)
C/T-R (95)	8	81.1	>16	84.2	>16	61.1	—	—	32	84.2	16	65.3	≤1	98.9	2	93.7	(>8)	(85.3)
I/R-R (33)	16	54.5	>16	57.6	>16	6.1	>32	0	>32	54.5	—	—	≤1	97	16	81.8	(1)	(90.9)
CST-R (32)	4	81.3	>16	87.5	1	90.6	>32	56.3	0.5	90.6	2	90.6	≤1	100	2	93.8	—	—

Results are not reported for isolates tested against antibiotics to which they had an expected resistance phenotype. Susceptibility was assessed according to EUCAST breakpoints (including high dosage breakpoints and breakpoints for the agent without inhibitor, where necessary), except CST, for which ECOFF values were used to define the proportion of isolates that could be considered wild-type strains (ie, those without phenotypically detectable acquired resistance mechanisms). Data are shown where n≥20 isolates were available. Data on susceptibility to CST are shown in parentheses as CST is not recommended for monotherapy and is not associated with a clinical monotherapy breakpoint (as per EUCAST v.14.0 guidance).

Abbreviations: ATM/AVI, aztreonam–avibactam; CST, colistin; C/T, ceftolozane–tazobactam; CZA, ceftazidime–avibactam; ECOFF, epidemiological cut-off; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FEP/TAN, cefepime–taniborbactam; I/R, imipenem–relebactam; MEM, meropenem; MVB, meropenem–vaborbactam; R, resistant; S, susceptibility.

[a]With the exception of cefiderocol-R isolates, I/R data exclude Morganellaceae (MEM-R, n=146; CZA-R, n=94; C/T-R, n=408; MVB-R, n=47; I/R-R, n=95; and FEP/TAN-R, n=22); CST data exclude Morganellaceae and *Serratia* spp. (cefiderocol-R, n=36; MEM-R, n=146; CZA-R, n=94; C/T-R, n=404; MVB-R, n=47; I/R-R, n=91; and FEP/TAN-R, n=20).

Table adapted from Santerre Henriksen et al. *Microbiol Spectr.* 2024.

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In Vitro Studies (Cont.)

Table 8. *In Vitro* Activity of Cefiderocol, Other Antibiotics, and Antibiotic Combinations Tested against *P. aeruginosa* and *Acinetobacter* spp. Isolates with Resistant Phenotypes[8]

Isolate (n)	Susceptibility[a] (%)									
	Cefiderocol	MEM	CZA	C/T	MVB	I/R	ATM/AVI	FEP/TAN	SUL/DUR	(CST)
P. aeruginosa (950)	98.9	85.4	90.1	89.1	87.2	83.3	86.2	91.4	NA	(99.7)
MEM-R (139)	97.8	—	56.8	55.4	12.2	12.2	41.7	59.7	NA	(100)
CZA-R (94)	93.6	36.2	—	36.2	39.4	37.2	54.3	55.3	NA	(100)
C/T-R (104)	94.2	40.4	42.3	—	45.2	36.5	64.4	59.6	NA	(100)
MVB-R (122)	97.5	0	53.3	53.3	—	10.7	38.5	59	NA	(100)
I/R-R (159)	98.1	23.3	62.9	58.5	31.4	—	54.1	64.8	NA	(100)
ATM/AVI-R (131)	95.4	38.2	67.2	71.8	42.7	44.3	—	61.8	NA	(100)
FEP/TAN-R (82)	95.1	31.7	48.8	48.8	39	31.7	39	—	NA	(100)
MEM-R & CZA-R (60)	96.7	—	—	28.3	5	8.3	45	43.3	NA	(100)
MEM-R & C/T-R (62)	98.4	—	30.6	—	8.1	9.7	54.8	50	NA	(100)
Acinetobacter spp. (501)[b]	92.4	54.7	NA	NA	NA	NA	NA	NA	97	(98.4)
Cefiderocol-R (38)	—	10.5	NA	NA	NA	NA	NA	NA	65.8	(92.1)
MEM-R (227)	85	—	NA	NA	NA	NA	NA	NA	93.8	(97.4)
SUL/DUR-R[c] (15)	13.3	6.7	NA	NA	NA	NA	NA	NA	—	(100)

Antimicrobials were tested against *P. aeruginosa* and/or *Acinetobacter* spp. based on expected use in a real-world setting. Results are not reported for isolates tested against antibiotics to which they had an expected resistance phenotype. Susceptibility was assessed according to EUCAST breakpoints (including non-species-specific PK/PD breakpoints, high-dosage breakpoints, and breakpoints for the agent without inhibitor, where applicable), except for SUL/DUR and CST where FDA breakpoints and ECOFF values were used, respectively. Data are shown where n≥20 isolates were available. Data on susceptibility to CST are shown in parentheses as CST is not recommended for monotherapy and is not associated with a clinical monotherapy breakpoint (as per EUCAST v.14.0 guidance).

Abbreviations: ATM/AVI, aztreonam–avibactam; CST, colistin; C/T, ceftolozane–tazobactam; CZA, ceftazidime–avibactam; ECOFF, epidemiological cut-off; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FDA, Food and Drug Administration; FEP/TAN, cefepime–taniborbactam; I/R, imipenem–relebactam; MEM, meropenem; MVB, meropenem–vaborbactam; NA, not applicable; PD, pharmacodynamic; PK, pharmacokinetic; R, resistant; SUL/DUR, sulbactam–durlobactam.

[a]Refers to susceptibility, or susceptibility with increased exposure for MEM, MVB, ATM/AVI, and FEP/TAN.

[b]Includes 458 *A. baumannii* complex isolates.

[c]SUL/DUR-R isolates were included irrespective of the number of isolates due to the scarcity of published data.

Table adapted from Santerre Henriksen et al. *Microbiol Spectr.* 2024.

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In Vitro 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. 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.[9]

Results[9]

- 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 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 9** shows the comparison of cefiderocol MICs against isolates collected before and after treatment with BL–BLIs
- Cefiderocol MIC_{50} and MIC_{90} in the ceftolozane–tazobactam (n=58) and ceftazidime–avibactam (n=59) NS isolates was 0.25 and 4 mg/L, respectively. In imipenem–relebactam (n=40) NS isolates, cefiderocol MIC_{50} was 0.25 mg/L and MIC_{90} was 2 mg/L
  - The median MIC for cefiderocol doubled from 0.12 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, 3/21 (14%) isolates developed a cefiderocol MIC >4 mg/L following exposure to ceftolozane–tazobactam

Table 9. Comparison of Cefiderocol MIC Values against Isolates Collected Before and After Treatment with Ceftolozane–Tazobactam, Ceftazidime–Avibactam or Imipenem–Relebactam[9]

		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 to 32	64	256	4 to 256	<0.0001
	Ceftolozane–tazobactam	2	4	0.25 to 8	64	256	1 to >64	<0.0001
	Cefiderocol	0.12	1	≤0.03 to 2	0.5	8	≤0.03 to 16	0.1034
	Imipenem–relebactam	2	8	≤0.06 to 8	2	4	0.25 to 32	0.6692
	Meropenem–vaborbactam	8	32		16	32	0.5 to 64	0.252
		n=			n=9			
Ceftazidime–avibactam exposure	Ceftazidime–avibactam	4	8		16	64	4 to 128	0.0238
	Ceftolozane–tazobactam	2	2		4	16	2 to 16	0.0280
	Cefiderocol	0.06	0.12		0.06	0.25	≤0.03 to 0.25	>0.9999
	Imipenem–relebactam	1	1		1	4	0.12 to 8	0.4965
	Meropenem–vaborbactam	32	64	8 to 64	8	32	2 to 32	0.0909
		n=12			n=17			
Imipenem–relebactam exposure	Ceftazidime–avibactam	8	128	4 to 256	32	128	8 to 256	0.1986
	Ceftolozane–tazobactam	16	128	1 to >64	8	64	1 to >64	0.4307
	Cefiderocol	0.25	1	0.12 to 2	0.5	2	0.06 to 2	0.4038
	Imipenem–relebactam	1	2	0.25 to 2	4	16	2 to 32	<0.0001
	Meropenem–vaborbactam	8	16	2 to 32	16	64	8 to 64	0.0007

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In Vitro Studies (Cont.)

Table 9. Comparison of Cefiderocol MIC Values against Isolates Collected Before and After Treatment with Ceftolozane–Tazobactam, Ceftazidime–Avibactam or Imipenem–Relebactam[9]

		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 to 32	64	256	4 to 256	<0.0001
	Ceftolozane–tazobactam	2	4	0.25 to 8	64	256	1 to >64	<0.0001
	Cefiderocol	0.12	1	≤0.03 to 2	0.5	8	≤0.03 to 16	0.1034
	Imipenem–relebactam	2	8	≤0.06 to 8	2	4	0.25 to 32	0.6692
	Meropenem–vaborbactam	8	32	1 to 32	16	32	0.5 to 64	0.252
		n=4			n=9			
Ceftazidime–avibactam exposure	Ceftazidime–avibactam	4	8	1 to 8	16	64	4 to 128	0.0238
	Ceftolozane–tazobactam	2	2	1 to 2	4	16	2 to 16	0.0280
	Cefiderocol	0.06	0.12	≤0.03 to 0.12	0.06	0.25	≤0.03 to 0.25	>0.9999
	Imipenem–relebactam	1	1	0.25 to 1	1	4	0.12 to 8	0.4965
	Meropenem–vaborbactam	32	64	8 to 64	8	32	2 to 32	0.0909
		n=12			n=17			
Imipenem–relebactam exposure	Ceftazidime–avibactam	8	128	4 to 256	32	128	8 to 256	0.1986
	Ceftolozane–tazobactam	16	128	1 to >64	8	64	1 to >64	0.4307
	Cefiderocol	0.25	1	0.12 to 2	0.5	2	0.06 to 2	0.4038
	Imipenem–relebactam	1	2	0.25 to 2	4	16	2 to 32	<0.0001
	Meropenem–vaborbactam	8	16	2 to 32	16	64	8 to 64	0.0007

MIC_{50} and MIC_{90} values are rounded to the nearest doubling dilution.
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.

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In Vitro Studies (Cont.)

Poirel et al (2022) evaluated 2 previously identified KPC-3 variants of *K. pneumoniae* from clinical isolates that conferred high-level resistance to ceftazidime–avibactam. These isolates were *K. pneumoniae* KPC-41 and KPC-50, both having distinct 3-amino acid-insertions in KPC β-lactamase. MICs were assessed by broth microdilution in ID-CAMHB for cefiderocol, and in CAMHB for ceftazidime–avibactam. Susceptibility was evaluated according to EUCAST breakpoints.[10]

Results[10]

- The MICs for cefiderocol and ceftazidime–avibactam against *K. pneumoniae* KPC-3, KPC-41, and KPC-50 are shown in **Table 10**
- Both KPC variants were resistant to cefiderocol and ceftazidime–avibactam according to the breakpoints, >2 and >8 µg/mL, respectively (**Table 10**)
- To account for potential mutations in the clinical strains that could be contributing to resistance, recombinant plasmids containing the 2 mutated KPC genes were introduced into a wild-type laboratory strain, *E. coli* TOP10
- Similar resistance patterns for both cefiderocol and ceftazidime–avibactam with respect to TOP10 (pKPC-41), but not TOP10 (pKPC-50) were revealed (**Table 10**)
- The MIC of cefiderocol against the recombinant strain containing KPC-50 was identical to that of the parent strain containing KPC-3, suggesting that an independent mutation in *K. pneumoniae* KPC-50 contributed to cefiderocol resistance

Table 10. MICs of Cefiderocol and Ceftazidime–Avibactam against Clinical and Recombinant Strains Containing KPC-3, KPC-41, and KPC-50[10]

Strain	MIC (µg/mL)	
	Cefiderocol	Ceftazidime–Avibactam
K. pneumoniae KPC-3	2	4
K. pneumoniae KPC-41	4–8	>128
K. pneumoniae KPC-50		>256
E. coli TOP10 (pTOPO-KPC-3)		2
E. coli TOP10 (pTOPO-KPC-41)		128
E. coli TOP10 (pTOPO-KPC-50)	1	64
E. coli TOP10	≤0.125	0.25

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In Vitro Studies (Cont.)

Table 10. MICs of Cefiderocol and Ceftazidime–Avibactam against Clinical and Recombinant Strains Containing KPC-3, KPC-41, and KPC-50[10]

Strain	MIC (µg/mL)	
	Cefiderocol	Ceftazidime–Avibactam
K. pneumoniae KPC-3	2	4
K. pneumoniae KPC-41	4–8	>128
K. pneumoniae KPC-50	16	>256
E. coli TOP10 (pTOPO-KPC-3)	1	2
E. coli TOP10 (pTOPO-KPC-41)	4	128
E. coli TOP10 (pTOPO-KPC-50)	1	64
E. coli TOP10	≤0.125	0.25

Abbreviations: KPC, *K. pneumoniae* carbapenemase; MIC, minimum inhibitory concentration.
Table adapted from Poirel et al. *Eur J Clin Microbiol Infect Dis*. 2022.

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In Vitro Studies (Cont.)

Werth et al (2022) conducted a serial passage study of 3 independent *S. maltophilia* strains. *S. maltophilia* is intrinsically resistant to many antibiotics due to innate resistance mechanisms, including chromosomally located genes that code for a class A serine β-lactamase and class B MBLs. The 3 independent strains (blood isolates) were sequentially passaged on media containing increasing concentrations of cefiderocol. Isolated cefiderocol-NS colonies were derived from each of the 3 *S. maltophilia* strains. To determine cross-resistance, the isolates were subsequently tested for susceptibility to cefiderocol and other antibiotics. MICs were determined by broth microdilution for cefiderocol, minocycline, trimethoprim–sulfamethoxazole, and ceftazidime, and by MIC test strip for ceftazidime–avibactam.[11]

Results[11]

- The results of susceptibility testing of cefiderocol-NS *S. maltophilia* isolates are shown in **Table 11**
- Isolates with reduced susceptibility to cefiderocol that were cross-resistant to ceftazidime–avibactam were observed
- Limited cross-resistance to other antibiotics was seen, however, a 4-fold decrease in trimethoprim–sulfamethoxazole MICs was observed in derivatives from 2 of the 3 strains (W357 and W364)

Table 11. MICs of Cefiderocol and Ceftazidime–Avibactam against Clinical and Recombinant Strains Containing KPC-3, KPC-41, and KPC-50[11]

Strain	MIC (µg/mL)				
	Cefiderocol	Ceftazidime–Avibactam	Ceftazidime	Minocycline	Trimethoprim–Sulfamethoxazole
W357-Parent	0.03125	4	128	4	0.5/9.5
W357-2-10	32	≥256	256	2	0.125/2.375
W358-Parent	0.125	64	[illegible]	0.5	0.125/2.375
W358-1-25	32	≥256	[illegible]	0.5	0.25/4.75
W358-2-2	8	≥256	≥256	0.5	0.125/2.375
W358-2-15	16	≥256	≥256	0.5	0.25/4.75
W364-Parent	0.03125	48	64–128	1	1/19
W364-8	8	≥256	256	1	0.25/4.75

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In Vitro Studies (Cont.)

Table 11. Changes in MICs to Several Antibiotics of *S. maltophilia* Isolates from Serial Passage Experiments[11]

Strain	MIC (µg/mL)				
	Cefiderocol	Ceftazidime–Avibactam	Ceftazidime	Minocycline	Trimethoprim–Sulfamethoxazole
W357-Parent	0.03125	4	128	4	0.5/9.5
W357-2-10	32	≥256	256	2	0.125/2.375
W358-Parent	0.125	64	≥256	0.5	0.125/2.375
W358-1-25	32	≥256	≥256	0.5	0.25/4.75
W358-2-2	8	≥256	≥256	0.5	0.125/2.375
W358-2-15	16	≥256	≥256	0.5	0.25/4.75
W364-Parent	0.03125	48	64–128	1	1/19
W364-8	8	≥256	256	1	0.25/4.75

Abbreviation: MIC, minimum inhibitory concentration.
Table adapted from Werth et al. *JAC Antimicrob Resist*. 2022.

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In Vitro Studies (Cont.)

Lasarte-Monterrubio et al (2022) evaluated 30 MDR/XDR *P. aeruginosa* strains resistant to ceftolozane–tazobactam and ceftazidime–avibactam due to various β-lactamases (variants of PDC, OXA-2, OXA-10), collected from multiple hospitals in Spain. Samples were collected from patients either before, during, or after treatment and were exposed to various antibiotics, including cefiderocol. Susceptibility was evaluated based on EUCAST breakpoints.[12]

Results[12]

- Many had MICs ranges of 8 to ≥512 mg/L for both ceftazidime–avibactam and ceftolozane–tazobactam
- Cefiderocol was active against 29 of the 30 isolates, with a susceptibility rate of 96.6%
  - MIC range was ≤0.12 to 2 mg/L
  - 1 isolate harboring mutations in PBP-3 and over-expressed MexAB-OprM, as well as PDC-221 variant, was NS (MIC=16 mg/L)
- Overall, cefiderocol was active against PDC-over-producing strains (MIC range of 0.25 to 2 mg/L), with lower activity against OXA-15, OXA-539, and OXA-681 over-producing strains (all had MICs=4 mg/L)

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In Vitro Studies (Cont.)

Karlowsky et al (2022) reported on the *in vitro* activity of cefiderocol against Gram-negative clinical isolates, including *P. aeruginosa*, *A. baumannii*, Enterobacterales, and others, collected from North America and Europe in 5 multinational surveillance studies (SIDERO-WT-2014 to 2019).[13]

- *In vitro* activity was assessed for cefiderocol, ceftazidime–avibactam, ceftolozane–tazobactam, and other agents against all isolates, meropenem-NS isolates, ceftazidime–avibactam-NS isolates, and ceftazidime–tazobactam-NS isolates
- A breakdown of susceptibility results of cefiderocol, ceftazidime–avibactam, and ceftolozane–tazobactam against these various pathogens is presented in **Table 12**

Table 12. Susceptibility Testing Results from SIDERO-WT Surveillance Study (2014–2019) Isolates of Enterobacterales, *P. aeruginosa*, and *A. baumannii* from North America and Europe[13]

Organism/Phenotype (No. of Isolates)	Antimicrobial Agent(s)	MIC (µg/mL)			CLSI MIC Interpretation[a]		
		Range	MIC_{50}	MIC_{90}	%S	%I	%R
Enterobacterales							
All isolates (31,896)	Cefiderocol	≤0.002 to >256	0.12	1	99.8	0.2	0.1
	Ceftazidime–avibactam	≤0.03 to >64	0.12	0.5	99.2	NA	0.8
	Ceftolozane–tazobactam	≤0.06 to >64	0.25	2	91.7	1.8	6.6
Meropenem-NS (MIC ≥2 mg/mL) (1021)	Cefiderocol	0.004 to >256	1	4	96.7	2.6	0.8
	Ceftazidime–avibactam	≤0.06 to >64	1	>64	77	NA	23
	Ceftolozane–tazobactam	0.25 to >64	64	>64	7.8	2.9	89.2
Ceftazidime–avibactam-NS (MIC ≥16 mg/mL) (263)	Cefiderocol	0.015 to >256	2	4	91.6	5.3	3
	Ceftazidime–avibactam	16 to >64	>64	>64	0	NA	100
	Ceftolozane–tazobactam	0.12 to >64	>64	>64	3.8	0.4	95.8
Ceftolozane–tazobactam-NS (MIC ≥4 mg/mL) (2658)	Cefiderocol	0.004 to >256	1	4	97.7	1.7	0.6
	Ceftazidime–avibactam	≤0.06 to >64	1	8	90.5	NA	9.5
	Ceftolozane–tazobactam	[illegible]	16	>64	0	21.3	78.7
P. aeruginosa							
All isolates (7700)	Cefiderocol	[illegible]	0.12	0.5	99.9	0.1	0
	Ceftazidime–avibactam	[illegible]	2	8	93.8	NA	6.2
	Ceftolozane–tazobactam	[illegible]	0.5	2	94	1	5
Meropenem-NS (MIC ≥4 mg/mL) (1759)	Cefiderocol	≤[illegible]	0.25	1	99.8	0.2	0
	Ceftazidime–avibactam	≤0.06 to >64	4	32	75	NA	25
	Ceftolozane–tazobactam	0.25 to >64	1	>64	76.1	3.3	20.6
Ceftazidime–avibactam-NS (MIC ≥16 mg/mL) (477)	Cefiderocol	≤0.002 to 4	0.25	2	100	0	0
	Ceftazidime–avibactam	16 to >64	32	>64	0	NA	100
	Ceftolozane–tazobactam	0.5 to >64	64	>64	24.3	6.5	69.2
Ceftolozane–tazobactam-NS (MIC ≥8 mg/mL) (463)	Cefiderocol	0.004 to 8	0.25	2	99.8	0.2	0
	Ceftazidime–avibactam	0.5 to >64	32	>64	22	NA	78
	Ceftolozane–tazobactam	8 to >64	64	>64	0	16.9	83.2
A. baumannii complex							
All isolates (5225)	Cefiderocol	≤0.002 to >256	0.12	1	96	1.3	2.7
	Ceftazidime–avibactam	≤0.06 to >64	16	>64	NA	NA	NA
	Ceftolozane–tazobactam	≤0.06 to >64	8	>64	NA	NA	NA
Meropenem-NS (MIC ≥4 mg/mL) (2810)	Cefiderocol	≤0.002 to >256	0.25	2	94.2	2.1	3.7
	Ceftazidime–avibactam	1 to >64	32	>64	NA	NA	NA
	Ceftolozane–tazobactam	≤0.06 to >64	16	>64	NA	NA	NA

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In Vitro Studies (Cont.)

Table 12. Susceptibility Testing Results from SIDERO-WT Surveillance Study (2014–2019) Isolates of Enterobacterales, *P. aeruginosa*, and *A. baumannii* from North America and Europe[13]

Organism/Phenotype (No. of Isolates)	Antimicrobial Agent(s)	MIC (µg/mL)			CLSI MIC Interpretation[a]		
		Range	MIC_{50}	MIC_{90}	%S	%I	%R
Enterobacterales							
All isolates (31,896)	Cefiderocol	≤0.002 to >256	0.12	1	99.8	0.2	0.1
	Ceftazidime–avibactam	≤0.03 to >64	0.12	0.5	99.2	NA	0.8
	Ceftolozane–tazobactam	≤0.06 to >64	0.25	2	91.7	1.8	6.6
Meropenem-NS (MIC ≥2 mg/mL) (1021)	Cefiderocol	0.004 to >256	1	4	96.7	2.6	0.8
	Ceftazidime–avibactam	≤0.06 to >64	1	>64	77	NA	23
	Ceftolozane–tazobactam	0.25 to >64	64	>64	7.8	2.9	89.2
Ceftazidime–avibactam-NS (MIC ≥16 mg/mL) (263)	Cefiderocol	0.015 to >256	2	4	91.6	5.3	3
	Ceftazidime–avibactam	16 to >64	>64	>64	0	NA	100
	Ceftolozane–tazobactam	0.12 to >64	>64	>64	3.8	0.4	95.8
Ceftolozane–tazobactam-NS (MIC ≥4 mg/mL) (2658)	Cefiderocol	0.004 to >256	1	4	97.7	1.7	0.6
	Ceftazidime–avibactam	≤0.06 to >64	1	8	90.5	NA	9.5
	Ceftolozane–tazobactam	4 to >64	16	>64	0	21.3	78.7
P. aeruginosa							
All isolates (7700)	Cefiderocol	≤0.002 to 8	0.12	0.5	99.9	0.1	0
	Ceftazidime–avibactam	≤0.03 to >64	2	8	93.8	NA	6.2
	Ceftolozane–tazobactam	≤0.06 to >64	0.5	2	94	1	5
Meropenem-NS (MIC ≥4 mg/mL) (1759)	Cefiderocol	≤0.002 to 8	0.25	1	99.8	0.2	0
	Ceftazidime–avibactam	≤0.06 to >64	4	32	75	NA	25
	Ceftolozane–tazobactam	0.25 to >64	1	>64	76.1	3.3	20.6
Ceftazidime–avibactam-NS (MIC ≥16 mg/mL) (477)	Cefiderocol	≤0.002 to 4	0.25	2	100	0	0
	Ceftazidime–avibactam	16 to >64	32	>64	0	NA	100
	Ceftolozane–tazobactam	0.5 to >64	64	>64	24.3	6.5	69.2
Ceftolozane–tazobactam-NS (MIC ≥8 mg/mL) (463)	Cefiderocol	0.004 to 8	0.25	2	99.8	0.2	0
	Ceftazidime–avibactam	0.5 to >64	32	>64	22	NA	78
	Ceftolozane–tazobactam	8 to >64	64	>64	0	16.9	83.2
A. baumannii complex							
All isolates (5225)	Cefiderocol	≤0.002 to >256	0.12	1	96	1.3	2.7
	Ceftazidime–avibactam	≤0.06 to >64	16	>64	NA	NA	NA
	Ceftolozane–tazobactam	≤0.06 to >64	8	>64	NA	NA	NA
Meropenem-NS (MIC ≥4 mg/mL) (2810)	Cefiderocol	≤0.002 to >256	0.25	2	94.2	2.1	3.7
	Ceftazidime–avibactam	1 to >64	32	>64	NA	NA	NA
	Ceftolozane–tazobactam	≤0.06 to >64	16	>64	NA	NA	NA

Abbreviations: CLSI, Clinical and Laboratory Standards Institute; I, intermediate; MIC, minimum inhibitory concentration; NA, not applicable; NS, non-susceptible; R, resistant; S, susceptible.
Table adapted from Karlowsky et al. *Antimicrob Agents Chemother*. 2022.

Fetroja® – Cross-Resistance to Other Antibiotics

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In Vitro Studies (Cont.)

Bianco et al (2022) investigated the *in vitro* activity of cefiderocol against KPC-producing Enterobacterales (N=100), including clinical isolates susceptible or resistant to ceftazidime–avibactam, derived from a tertiary care teaching hospital in Italy. Susceptibility to cefiderocol was assessed by broth microdilution and disk diffusion testing. Susceptibility to ceftazidime–avibactam was determined by a gradient diffusion method and evaluated based on EUCAST breakpoints.[14]

Results[14]

- Of the 100 isolates collected, 60 were susceptible to ceftazidime–avibactam, including *K. pneumoniae* (n=57), *E. coli* (n=1), *Klebsiella oxytoca* (n=1), and *S. marcescens* (n=1) and 40 (all *K. pneumoniae*) were resistant to ceftazidime–avibactam
- Cefiderocol resistance was significantly higher in isolates resistant to ceftazidime–avibactam compared with those that were susceptible (P<0.001):
  - Resistance rate by broth microdilution: 82.5% versus 6.7%, respectively
  - Resistance rate by disk diffusion: 82.5% versus 13.3%, respectively
- Cefiderocol $MIC_{50/90}$ values were 0.25 and 2 µg/mL, respectively, against ceftazidime–avibactam-susceptible isolates and 8 and 64 µg/mL, respectively, against ceftazidime–avibactam-resistant isolates
- KPC-Kp isolates harboring KPC-D179Y (n=5) or KPC-2-Δ242-GT-243 (n=2) variants demonstrated MICs ranging from 4 to 64 µg/mL

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In Vitro Studies (Cont.)

Simner et al (2021) assessed the frequency of non-susceptibility to cefiderocol in a group of patients who were treated with ceftolozane–tazobactam for DTR *P. aeruginosa*. 16 paired isolates of DTR *P. aeruginosa* were obtained from patients before and after treatment with ceftolozane–tazobactam. All 16 isolates were susceptible to ceftolozane–tazobactam and cefiderocol prior to treatment with ceftolozane–tazobactam. Susceptibility to cefiderocol and ceftolozane–tazobactam for the 32 isolates was conducted by broth microdilution. CLSI criteria were used to evaluate susceptibility, with cefiderocol MICs of ≤4 µg/mL for *P. aeruginosa* considered susceptible.[15]

Results[15]

- 10 of the 16 pairs of strains demonstrated increases in ceftolozane–tazobactam MICs (ranging from 8 to 256 µg/mL) after treatment with ceftolozane–tazobactam. Of the 10, only 1 strain demonstrated an increase in cefiderocol MIC (from 0.25 to 8 µg/mL). Susceptibility of the latter strain to cefiderocol would be classified as intermediate
- 3 pairs of isolates developed ≥4-fold increases in MICs to cefiderocol. MICs increased from:
  - 0.5 to 2 µg/mL
  - 0.25 to 2 µg/mL
  - 0.12 to 1 µg/mL
- Despite the increases in MIC observed, all 3 strains (isolated after ceftolozane–tazobactam treatment) were still susceptible to cefiderocol
- The MIC increases could potentially be due to mutations discovered in *ampC* (β-lactamase), *ampD* (may lead to AmpC over-production), and *mexR* (negative regulator of MexAB-OprM efflux pump)

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Relevant Prescribing Information

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

- Complicated urinary tract infections (cUTIs), including pyelonephritis caused by the following susceptible Gram-negative microorganisms:
  - *Escherichia coli*
  - *Klebsiella pneumoniae*
  - *Proteus mirabilis*
  - *Pseudomonas aeruginosa*
  - *Enterobacter cloacae* complex

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

Fetroja is contraindicated in:[16]

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

Section 12.4 Microbiology of the **Fetroja Full Prescribing Information** states the following:[16]

- Cross-resistance with other classes of antibacterial drugs has not been identified; therefore, isolates resistant to other antibacterial drugs may be susceptible to cefiderocol.
- Cefiderocol has shown *in vitro* activity against isolates of *S. maltophilia* and a subset of isolates of Enterobacterales and *P. aeruginosa* that are resistant to meropenem, ciprofloxacin, amikacin, cefepime, ceftazidime-avibactam, and ceftolozane/tazobactam. Cefiderocol has shown *in vitro* activity against subset of isolates of *A. baumannii* complex that are resistant to meropenem, ciprofloxacin, and amikacin. Cefiderocol is active against some colistin-resistant *E. coli* isolates containing *mcr-1*.

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

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Literature Search

As of May 2025, a computerized search of the published medical literature using internal and external databases (ie, Medline®, Embase®, and PubMed®) has identified several additional relevant references regarding cross-resistance of cefiderocol to other antibiotics. For your review, these references are listed in the bibliography below:

- Bianco G, Boattini M, Comini S, Gibellini D, Gaibani P. *In vivo* emergence of ceftazidime/avibactam, cefiderocol and aztreonam/avibactam cross-resistance in a patient with KPC-producing *Klebsiella pneumoniae* infection after cefiderocol-based treatment. *Int J Antimicrob Agents*. 2024;64(5):107343. [Web Link]
- Haidar G, Kline EG, Kitsios GD, et al. Emergence of high-level aztreonam-avibactam and cefiderocol resistance following treatment of an NDM-producing *Escherichia coli* bloodstream isolate exhibiting reduced susceptibility to both agents at baseline. *JAC Antimicrob Resist*. 2024;6(5):dlae141. [Web Link]
- Russo C, Mesini A, Mariani M, et al. Reduce susceptibility to cefiderocol in gram negative bacteria in children: is hope already lost before it's even arrived? *J Infect Public Health*. 2024;17(4):624-631. [Web Link]
- Galdino ACM, Vaillancourt M, Celedonio D, et al. Siderophores promote cooperative interspecies and intraspecies cross-protection against antibiotics *in vitro*. *Nat Microbiol*. 2024;9(3):631-646. [Web Link]
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- Klein S, Boutin S, Kocer K, et al. Rapid development of cefiderocol resistance in carbapenem-resistant *Enterobacter cloacae* during therapy is associated with heterogeneous mutations in the catecholate siderophore receptor cirA. *Clin Infect Dis*. 2022;74(5):905-908. [Web Link]
- 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]

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Literature Search (Cont.)

- Tiseo G, Falcone M, Leonildi A, et al. Meropenem-vaborbactam as salvage therapy for ceftazidime-avibactam-, cefiderocol-resistant ST-512 *Klebsiella pneumoniae*-producing KPC-31, a D179Y variant of KPC-3. *Open Forum Infect Dis*. 2021;8(6):ofab141. [Web Link]

- Hobson CA, Cointe A, Jacquier H, et al. Cross-resistance to cefiderocol and ceftazidime-avibactam in KPC β-lactamase mutants and the inoculum effect. *Clin Microbiol Infect*. 2021;27(8):1172.e7-1172.e10. [Web Link]

- Kawai A, McElheny CL, Iovleva A, et al. Structural basis of reduced susceptibility to ceftazidime-avibactam and cefiderocol in *Enterobacter cloacae* due to AmpC R2 loop deletion. *Antimicrob Agents Chemother*. 2020;64(7):e00198-20. [Web Link]

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

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Abbreviations

ACM	all-cause mortality	IV	intravenous
ADR	adverse drug reaction	I/R	imipenem–relebactam
AmpC	ampicillinase C	KPC	*K. pneumoniae* carbapenemase
ATM/AVI	aztreonam–avibactam	KPC-Kp	*K. pneumoniae* carbapenemase-producing *K. pneumoniae*
BL–BLI	β-lactam–β-lactamase inhibitor	MBL	metallo-β-lactamase
BMI	body mass index	MDR	multi-drug resistant
BSI	bloodstream infection	MEM	meropenem
CAMHB	cation-adjusted Mueller-Hinton broth	MER/VAB	meropenem–vaborbactam
Carb	carbapenem	MIC	minimum inhibitory concentration
Carb-NS	carbapenem-non-susceptible	MVB	meropenem–vaborbactam
CLSI	Clinical Laboratory Standards Institute	n	number
CR	carbapenem-resistant	NA	not applicable
CRE	carbapenem-resistant Enterobacterales	NS	non-susceptible
CST	colistin	OXA	oxacillinase
cUTI	complicated urinary tract infections	PBP-3	penicillin-binding protein-3
CZA	ceftazidime–avibactam	PD	pharmacodynamic
C/T	ceftolozane–tazobactam	PDC	*Pseudomonas*-derived cephalosporinase
DTR	difficult-to-treat	PIP/TAZ	piperacillin–tazobactam
EAP	Early Access Program	PK	pharmacokinetic
ECOFF	epidemiological cut-off	q8h	every 8 hours
ESRD	end-stage renal disease	R	resistant
EUCAST	European Committee on Antimicrobial Susceptibility Testing	RE	resistance emergent
FDA	US Food and Drug Administration	S	susceptible/susceptibility
FEP/TAN	cefepime–taniborbactam	SUL/DUR	sulbactam–durlobactam
g	grams	US	United States
h	hours	TOL/TAZ	ceftolozane–tazobactam
HABP	hospital-acquired bacterial pneumonia	VABP	ventilator-associated bacterial pneumonia
I	intermediate	VIM	Verona integron-mediated metallo-β-lactamase
ICU	intensive care unit	WGS	whole genome sequencing
ID-CAMHB	iron-depleted cation-adjusted Mueller-Hinton broth	XDR	extensively-drug resistant
IQR	interquartile range		

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

Enclosure

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