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Cefiderocol demonstrated potent *in vitro* activity against carbapenem-resistant non-fermenting Gram-negative bacteria, including WHO priority pathogens, in China

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INTRODUCTION

Cefiderocol, a siderophore cephalosporin, has demonstrated potent *in vitro* activity against aerobic Gram-negative bacteria, including carbapenem-resistant (CR) *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*, as well as other rare non-fermenting Gram-negative bacteria. In the USA, cefiderocol is approved for the treatment of adult patients with complicated urinary tract infections (cUTI) and hospital-acquired or ventilator-associated bacterial pneumonia. In Europe, cefiderocol is approved for the treatment of adult patients with serious Gram-negative bacterial infections with limited treatment options. In China, cefiderocol is currently approved for the treatment of adult patients with cUTI.

OBJECTIVES

The objective of the current surveillance study was to compare the *in vitro* activity of cefiderocol and comparator antimicrobial agents against CR Gram-negative non-fermenting bacteria collected in China.

METHODS

- Non-duplicate challenging non-fermenting Gram-negative bacterial isolates (N_{total}=833) were collected between 2019 and 2021 from hospitalised patients in 50 hospitals across 20 provinces across China. Isolates were collected within the China Antimicrobial Surveillance Network (CHINET), which collects annually bacterial isolates nationwide from routine clinical specimens, including blood, respiratory, urinary, intra-abdominal, and other samples.
- Cefiderocol susceptibility testing was performed by broth microdilution method according to the Clinical and Laboratory Standards Institute (CLSI) guidance, using pre-prepared ThermoFisher plates (Shanghai, China) with cation-adjusted Mueller-Hinton broth (CAMHB) for comparator antibiotics and iron-depleted CAMHB for cefiderocol.
- Minimum inhibitory concentrations (MICs) were interpreted according to 2025 CLSI breakpoints, except for colistin, which was interpreted according to EUCAST breakpoints. Carbapenem (i.e., meropenem) susceptibility was interpreted by CLSI 2025 breakpoints.

RESULTS

- Against 252 CR *A. baumannii* isolates, cefiderocol was the most active antibiotic with 99.6% susceptibility rate and $MIC_{50/90}$ values of 0.5/2 µg/mL (**Table 1**). Among comparators, only colistin was active with 99.2% susceptibility rate based on EUCAST breakpoint, and tigecycline inhibited 86.5% of isolates at 2 µg/mL.

Table 1. *In vitro* activities and susceptibilities to cefiderocol and comparators against CR *A. baumannii* (N=252)[a]

Antimicrobial agent0.4	MIC range (µg/mL)	MIC_{50} (µg/mL)	MIC_{90} (µg/mL)	% S (CLSI criteria)	% R (CLSI criteria)
Cefiderocol	≤0.03–16	0.5	2	99.6	0.4
Ceftazidime-avibactam	8–>32	>32	>32	–[c]	–
Ceftolozane-tazobactam	2–>32	32	>32	–	–
Imipenem-relebactam	16–>16	>16	>16	–	–
Ampicillin-sulbactam	16–>64	>64	>64	0	99.6
Meropenem	>16	>16	>16	0	100
Amikacin	1–>64	>64	>64	17.9	81.3
Levofloxacin	≤0.25–>8	>8	>8	1.6	98.4
Tigecycline	0.12–>8	2	4	–	–
Colistin[b]	≤0.25–>8	0.5	0.5	99.2	0.8
Cefepime	16–>32	>32	>32	0	98.8

CLSI, Clinical and Laboratory Standards Institute; CR, carbapenem-resistant; EUCAST, European Committee on Antimicrobial Susceptibility Testing; MIC, minimum inhibitory concentration; R, resistant; S, susceptible.
[a] bla_{OXA-23} gene was detected in 165 CR isolates by polymerase chain reaction, including two isolates with bla_{OXA-58} gene; the remaining 87 isolates had no carbapenemases; [b] EUCAST susceptibility breakpoints are applicable; [c] No breakpoints available.

- Against 254 CR *P. aeruginosa* isolates, cefiderocol showed very high *in vitro* activity with 98.4% susceptibility rate and $MIC_{50/90}$ values of 0.5/2 µg/mL (**Table 2**). Among comparators, susceptibility rates for colistin (99.2%) and amikacin (84.3%) were higher than for ceftazidime-avibactam (69.7%) and ceftolozane-tazobactam (78.7%).

Table 2. *In vitro* activities and susceptibilities to cefiderocol and comparators against CR *P. aeruginosa* (N=254)

Antimicrobial agent	MIC range (µg/mL)	MIC_{50} (µg/mL)	MIC_{90} (µg/mL)	% S (CLSI criteria)	% R (CLSI criteria)
Cefiderocol	≤0.03–>64	0.5	2	98.4	0.8
Ceftazidime-avibactam	2–>32	8	32	69.7	30.3
Ceftolozane-tazobactam	0.5–>32	2	>32	78.7	19.3
Imipenem-relebactam	0.25–>16	2	>16	56.3	23.6
Ampicillin-sulbactam	>64	>64	>64	–	–
Meropenem	8–>16	>16	>16	0	100
Amikacin	≤0.5–>64	4	64	84.3	12.6
Levofloxacin	≤0.25–>8	8	>8	20.9	70.9
Tigecycline	1–>8	8	>8	–	–
Colistin[a]	≤0.25–>8	0.5	1	99.2	0.8
Cefepime	≤0.25–>32	16	>32	34.3	38.2

CLSI, Clinical and Laboratory Standards Institute; CR, carbapenem-resistant; EUCAST, European Committee on Antimicrobial Susceptibility Testing; MIC, minimum inhibitory concentration; R, resistant; S, susceptible.
[a] EUCAST susceptibility breakpoints are applicable.

- Against 254 *Stenotrophomonas maltophilia* isolates, cefiderocol was the most active antibiotic agent tested, with nearly all isolates being susceptible (99.6% susceptibility) and very low $MIC_{50/90}$ values (0.06/0.125 µg/mL) compared with other antibiotic agents ($MIC_{50/90}$ ≥2/≥8 µg/mL) (**Table 3**).

Table 3. *In vitro* activities and susceptibilities to cefiderocol and comparators against *S. maltophilia* (N=254)

Antimicrobial agent	MIC range (µg/mL)	MIC_{50} (µg/mL)	MIC_{90} (µg/mL)	% S (CLSI criteria)	% R (CLSI criteria)
Cefiderocol	≤0.03–4	0.06	0.125	99.6	–
Ceftazidime-avibactam	0.5–>32	8	>32	–[a]	–
Ceftolozane-tazobactam	0.5–>32	16	>32	–	–
Imipenem-relebactam	2–>16	>16	>16	–	–
Ampicillin-sulbactam	8–>64	>64	>64	–	–
Meropenem	0.5–>16	>16	>16	–	–
Amikacin	4–>64	>64	>64	–	–
Levofloxacin	≤0.25–>8	2	>8	72.4	15.4
Tigecycline	0.25–>8	2	8	–	–
Colistin	≤0.25–>8	>8	>8	–	–
Cefepime	4–>32	>32	>32	–	–

CLSI, Clinical and Laboratory Standards Institute; MIC, minimum inhibitory concentration; R, resistant; S, susceptible.
[a] No breakpoints available.

- Against 73 *Burkholderia cepacia* isolates, cefiderocol displayed $MIC_{50/90}$ values of 0.06/0.25 µg/mL, and all isolates had MICs of ≤2 µg/mL (**Table 4**). Cefiderocol was the most active antibiotic *in vitro,* with lower MIC values than for any other comparator antibiotic.

Table 4. Minimum inhibitory concentrations of cefiderocol and comparators against *B. cepacia* (N=73)[a]

Antimicrobial agent	MIC range (µg/mL)	MIC_{50} (µg/mL)	MIC_{90} (µg/mL)
Cefiderocol	≤0.03–2	0.06	0.25
Ceftazidime-avibactam	0.5–16	4	8
Ceftolozane-tazobactam	0.25–>32	2	16
Imipenem-relebactam	0.25–>16	4	8
Ampicillin-sulbactam	≤2–>64	>64	> 64
Meropenem	≤0.06–>16	8	16
Amikacin	4–>64	>64	>64
Levofloxacin	0.5–>8	2	>8
Tigecycline	0.25–>8	4	8
Colistin	0.5–>8	>8	>8
Cefepime	2–>32	32	>32

CLSI, Clinical and Laboratory Standards Institute; MIC, minimum inhibitory concentration.
[a] 47 isolates (64.4%) were not susceptible to meropenem based on CLSI 2024 susceptibility breakpoints.

CONCLUSIONS

- Challenging CR non-fermenter isolates, including World Health Organization priority pathogens, collected in China were highly susceptible to cefiderocol, with all susceptibility rates approaching 100% for all species.
- These susceptibility rates are comparable to those previously described for CR non-fermenters collected in the USA and Europe.

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Conflict of interest

NK, XZ are employees of Shionogi China Ltd., Shanghai, China.
The other authors have no conflict of interest.

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