Poster 1484

IDWeek, October 16–19, 2024
Los Angeles, CA, USA

In vitro Activity of Cefiderocol and Comparator Agents Against Non-Fermenter Gram-Negative Bacilli Isolated from Patients Hospitalized with Pneumonia as Part of the SENTRY Global Surveillance Program (2020–2022)

Contact: Frank Kung
Email: frank.kung@shionogi.com

Frank Kung[1], Sean T. Nguyen[1], Boudewijn L.M. DeJonge[1], Chris Longshaw[2], Jason J. Bryowsky[1], Joshua M. Maher[3], Rodrigo E. Mendes[3], Miki Takemura[4], and Yoshinori Yamano[4]
[1]Shionogi Inc., Florham Park, New Jersey, USA; [2]Shionogi B.V., London, UK; [3]Element, North Liberty, Iowa, USA; [4]Shionogi & Co., Ltd., Osaka, Japan

SHIONOGI

BACKGROUND

- Cefiderocol is a siderophore conjugated cephalosporin with activity against a broad range of Gram-negative bacilli, including non-fermenters resistant to carbapenems.
- Cefiderocol is approved in the United States for the treatment of patients with complicated urinary tract infections and hospital-acquired/ventilator-associated bacterial pneumonia caused by susceptible Gram-negative pathogens and in Europe for the treatment of infections due to aerobic Gram-negative organisms in adults with limited treatment options.
- In this study, the *in vitro* activity of cefiderocol and comparators was evaluated against glucose non-fermenter Gram-negative bacteria isolated from patients hospitalized with pneumonia.

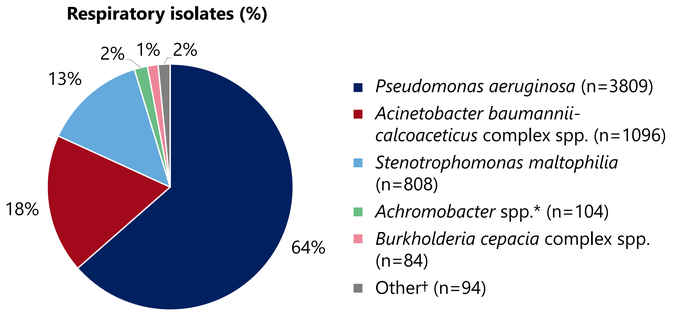
METHODS

- 5995 non-fermenter Gram-negative isolates were collected during 2020–2022 from patients with pneumonia as part of the Global SENTRY Antimicrobial Surveillance Program (**Figure 1**).
- Minimum inhibitory concentrations (MICs) were assessed using broth microdilution according to Clinical and Laboratory Standards Institute (CLSI) guidelines, with cation-adjusted Mueller–Hinton broth (CAMHB) for comparators and iron-depleted CAMHB for cefiderocol.
- Susceptibility was assessed according to 2024 CLSI, US Food and Drug Administration (FDA), and European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints.
- Carbapenem resistance (CR) was defined as resistant to meropenem and imipenem by CLSI breakpoints.

RESULTS

- Against *Pseudomonas aeruginosa*, cefiderocol and β-lactam–β-lactamase inhibitor combinations all showed susceptibility >95% (**Table 1**).
  - However, only cefiderocol maintained high susceptibility against CR *P. aeruginosa*, with 99.3% of the isolates being susceptible by CLSI breakpoints.
  - No other comparator had >90% susceptibility against CR *P. aeruginosa*.
- Against *Acinetobacter baumannii-calcoaceticus* complex, cefiderocol demonstrated 97.5% susceptibility by CLSI breakpoints (**Table 1**).
  - This high susceptibility was maintained against CR *A. baumannii-calcoaceticus* complex, with 96.1% susceptibility using CLSI breakpoints.
  - Colistin showed 75.3% susceptibility per EUCAST breakpoints, but ceftazidime and ampicillin-sulbactam showed <5% susceptibility.
- Cefiderocol, trimethoprim-sulfamethoxazole, and minocycline all showed >90% susceptibility against *Stenotrophomonas maltophilia* (**Table 1**).
- Against *Achromobacter* spp. and *Burkholderia cepacia* complex spp., cefiderocol had high activity, with $MIC_{50/90}$ values of 0.03/0.5 mg/L and 0.06/1 mg/L, respectively (**Figure 2**).

Figure 1. Distribution of non-fermenter Gram-negative bacilli (N=5995) from patients hospitalized with pneumonia as part of the SENTRY Global Surveillance Program (2020–2022)



*_Achromobacter_* spp. included: *Achromobacter denitrificans* (1), *Achromobacter insolitus* (2), *Achromobacter xylosoxidans* (14), and unspeciated *Achromobacter* (87).
†Other include *Acinetobacter beijerinckii* (1), *Acinetobacter bereziniae* (16), *Acinetobacter courvalinii* (2), *Acinetobacter dispersus* (2), *Acinetobacter guillouiae* (2), *Acinetobacter gyllenbergii* (1), *Acinetobacter haemolyticus* (1), *Acinetobacter johnsonii* (5), *Acinetobacter junii* (10), *Acinetobacter lwoffii* (2), *Acinetobacter modestus* (1), *Acinetobacter proteolyticus* (2), *Acinetobacter radioresistens* (2), *Acinetobacter soli* (1), *Acinetobacter ursingii* (24), *Burkholderia gladioli* (10), *Chryseobacterium arthrosphaerae* (1), *Chryseobacterium gleum* (1), *Chryseobacterium indologenes* (8), unspeciated *Acinetobacter* (1), unspeciated *Chryseobacterium* (1).

Figure 2. MIC distribution of cefiderocol against *Achromobacter* spp. and *Burkholderia cepacia* complex spp. from patients hospitalized with pneumonia in 2020–2022

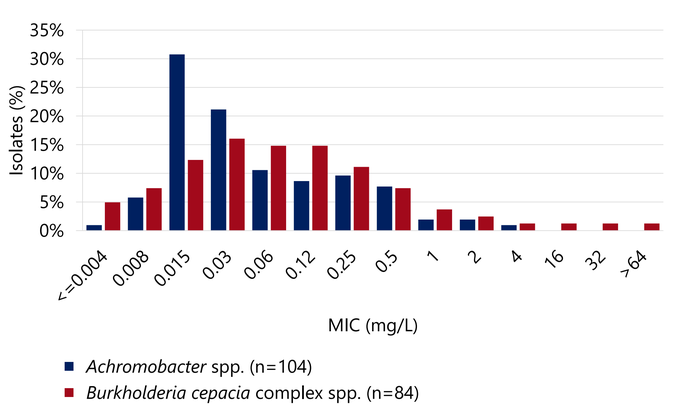


Table 1. Activity of cefiderocol and comparator agents against *Pseudomonas aeruginosa*, *Acinetobacter baumannii-calcoaceticus* complex, and *Stenotrophomonas maltophilia* isolates from patients hospitalized with pneumonia in 2020–2022

Agent	MIC_{50} (mg/L)	MIC_{90} (mg/L)	Range (mg/L)	CLSI[a] %S	FDA[a] %S	EUCAST[a] %S
P. aeruginosa **(N=3809)**						
Cefiderocol	0.06	0.25	≤0.004 to >64	99.7	98.3	99.3
Imipenem-relebactam	0.25	1	≤0.03 to >8	95.7	95.7	95.7
Ceftazidime-avibactam	2	8	≤0.015 to >32	95.9	95.9	95.9
Ceftolozane-tazobactam	0.5	2	≤0.12 to >16	95.5	95.5	95.5
Aztreonam-avibactam	4	>16	≤0.03 to >16	N/A	N/A	N/A
CR *P. aeruginosa* (n=588)						
Cefiderocol	0.12	0.5	≤0.004 to 16	99.3	96.1	98.6
Imipenem-relebactam	2	8	0.5 to >8	75.3	75.3	75.3
Ceftazidime-avibactam	4	32	0.5 to >32	81.6	81.6	81.6
Ceftolozane-tazobactam	1	16	0.25 to >16	81.8	81.8	81.8
Aztreonam-avibactam	16	>16	0.12 to >16	N/A	N/A	N/A
A. baumannii-calcoaceticus **complex (N=1096)**						
Cefiderocol	0.25	1	0.015 to >64	97.5	93.2	96.3
Ceftazidime	>32	>32	1 to >32	37.0	37.0	-
Ampicillin-sulbactam	32	>64	1 to >64	37.9	37.9	-
Colistin	0.5	>8	0.12 to >8	-	-	84.2
CR *A. baumannii-calcoaceticus* **complex (N=649)**						
Cefiderocol	0.25	1	0.015 to >64	96.1	90.4	94.1
Ceftazidime	>32	>32	4 to >32	3.4	3.4	N/A
Ampicillin-sulbactam	64	>64	4 to >64	2.2	2.2	N/A
Colistin	0.5	>8	0.12 to >8	N/A	N/A	75.3
S. maltophilia **(N=808)**						
Cefiderocol	0.06	0.25	0.008 to 4	99.1	N/A	99.8
Ceftazidime	>32	>32	0.12 to >32	N/A	16.6	N/A
Levofloxacin	1	4	≤0.015 to >32	83.4	N/A	N/A
Trimethoprim-sulfamethoxazole	≤0.12	0.5	≤0.12 to >4	96.9	N/A	N/A
Minocycline	0.5	1	≤0.06 to 8	93.4	N/A	N/A

N/A, not applicable; S, susceptible.
[a]Criteria as published by CLSI (2024), EUCAST (2024), and FDA (2024).

CONCLUSIONS

- Cefiderocol demonstrated high *in vitro* activity against glucose non-fermenters isolated from hospitalized patients with pneumonia.
- In particular, cefiderocol maintained high susceptibility against CR isolates, making it an important treatment option for patients with pneumonia who are at risk of infection with a CR non-fermenter.

Conflict of interest. FK, STN, BD, CL, JJB, MT, YY are employees of Shionogi. This study was funded by Shionogi & Co., Ltd., Osaka, Japan.