Poster 2112

IDWeek 2023, Boston, MA, USA
October 11–15, 2023

Contact: Jason J. Bryowsky
Email: jason.bryowsky@shionogi.com

In vitro Activity of Cefiderocol and Comparator Agents Against Enterobacterales from United States Hospitals Stratified by Infection Type (2020–2022)

Jason J. Bryowsky[1], Boudewijn L.M. DeJonge[1], Sean T. Nguyen[1], Josh Maher[2], Rodrigo E. Mendes[2], Miki Takemura[3], Yoshinori Yamano[3]
[1]Shionogi Inc., Florham Park, NJ, USA; [2]JMI Laboratories, North Liberty, IA, USA; [3]Shionogi & Co., Ltd., Osaka, Japan

Copies of this poster obtained through Quick Response (QR) Code are for personal use only and may not be reproduced without permission from IDWeek 2023 and the authors of the poster.

SHIONOGI

Introduction

- Cefiderocol is a siderophore-conjugated cephalosporin with broad activity against Gram-negative bacteria, including multidrug-resistant (MDR) organisms. Based on its unique structure and unique mode of cell entry, cefiderocol remains active against Gram-negative bacteria that employ mechanisms that commonly confer resistance to carbapenems.[1,2,3]

Objective

- To evaluate the *in vitro* activity of cefiderocol and comparator agents against Enterobacterales isolates collected during 2020–2022 in the SENTRY Antimicrobial Surveillance Program, stratified by infection type.

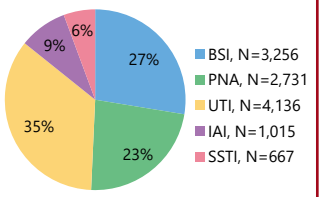
Methods

- Minimum inhibitory concentrations (MICs) were determined for 11,805 Enterobacterales from the USA, using Clinical and Laboratory Standards Institute (CLSI) broth microdilution method, with cation-adjusted Mueller–Hinton broth (CAMHB) for comparators and iron-depleted CAMHB for cefiderocol.
- Carbapenem-resistant Enterobacterales (CRE) was defined as resistance to imipenem and meropenem.
- MDR Enterobacterales was defined as non-susceptible to at least one drug from ≥3 classes, and extensively drug resistant (XDR) was defined as susceptible to ≤2 classes per 2022 CLSI criteria.

Results

- The most common infection type from which isolates were collected was urinary tract infection (UTI; N=4,136), followed by bloodstream infection (BSI; N=3,256), pneumonia (PNA; N=2,731), intra-abdominal infection (IAI; N=1,015), and skin and soft tissue infection (SSTI; N=667) (**Figure 1**).
- MDR was the most common phenotype observed, and the occurrence of CRE, MDR, and XDR phenotypes was highest among isolates from patients with pneumonia (**Figure 3**).
- Among CRE and MDR isolates, cefiderocol was the most active agent (>98% susceptible) for isolates from BSI, PNA, and UTI (**Table 1**).
- Among XDR isolates from BSI and PNA, susceptibility to cefiderocol was the highest (>97%) among all agents tested (**Table 1**).
- Of the β-lactam/β-lactamase inhibitor agents, ceftolozane-tazobactam and piperacillin-tazobactam demonstrated the lowest susceptibility rate for CRE and MDR isolates from BSI, PNA, UTI, and among XDR isolates from BSI and PNA (**Table 1**).

Figure 1. Infection type distribution (N=11,805)



Conclusions

Cefiderocol demonstrated high *in vitro* activity against Enterobacterales, regardless of infection type.

Susceptibility for comparator agents was generally lower against CRE, MDR and XDR phenotypes.

Cefiderocol represents a potential early treatment option for infections caused by Enterobacterales with presumed or defined CRE, MDR, XDR phenotypes, regardless of infection type.

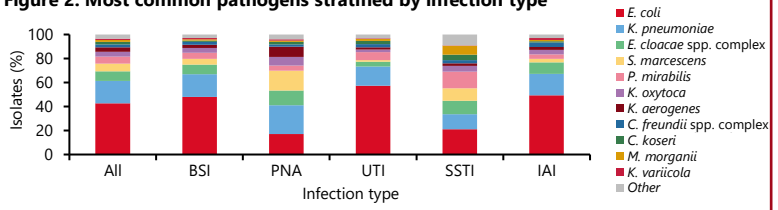
References: 1. Ito A, et al. Antimicrob Agents Chemother. 2018;62(1):e01454-17; **2.** Kazmierczak KM, et al. Int J Antimicrob Agents. 2019;53(2):177–184; **3.** Fetroja (cefiderocol) [package insert]. Florham Park, NJ: Shionogi Inc.; 2021.

Results

Table 1. *In vitro* activity of cefiderocol and comparators stratified by infection type from US hospitals 2020–2022

Phenotype/ Antimicrobial agent	Percent susceptible per CLSI criteria				
	BSI	PNA	UTI	SSTI	IAI
Enterobacterales	N=3,256	N=2,731	N=4,136	N=667	N=1,015
Cefiderocol	99.8	99.8	100	99.7	99.5
Cefepime	86.7	86.0	90.1	87.4	90.0
Ceftazidime	84.5	80.4	88.5	84.4	86.1
Meropenem	99.2	97.7	99.5	98.8	99.2
Piperacillin-tazobactam	89.5	80.1	91.9	87.0	86.9
Ceftazidime-avibactam	99.8	99.7	99.9	99.9	99.8
Ceftolozane-tazobactam	95.4	89.4	96.3	93.0	92.8
Imipenem-relebactam	95.9	95.7	94.2	86.4	97.0
Meropenem-vaborbactam	99.7	99.8	99.9	99.9	99.9
CRE	N=16	N=55	N=14	N=6	N=6
Cefiderocol	100	98.2	100	100	83.3
Ceftazidime-avibactam	87.5	94.5	78.6	83.3	83.3
Ceftolozane-tazobactam	0.0	7.3	0.0	0.0	0.0
Imipenem-relebactam	50.0	85.5	71.4	83.3	83.3
Meropenem-vaborbactam	50.0	90.9	71.4	83.3	83.3
MDR Enterobacterales	N=295	N=309	N=236	N=65	N=62
Cefiderocol	98.6	99.4	100	96.9	95.2
Cefepime	12.5	22.3	18.2	20.0	17.7
Ceftazidime	10.8	17.5	16.1	16.9	12.9
Meropenem	91.5	80.3	90.7	87.7	87.1
Piperacillin-tazobactam	44.6	27.2	40.7	36.9	32.3
Ceftazidime-avibactam	98.6	98.4	98.7	98.5	98.4
Ceftolozane-tazobactam	74.1	60.7	72.5	64.6	56.5
Imipenem-relebactam	96.3	93.2	94.9	93.8	98.4
Meropenem-vaborbactam	96.9	98.4	98.3	98.5	98.4
XDR Enterobacterales	N=19	N=35	N=9	N=6	N=2
Cefiderocol	100	97.1	100	100	50.0
Cefepime	0.0	2.9	0.0	0.0	0.0
Ceftazidime	0.0	2.9	0.0	0.0	0.0
Meropenem	10.5	5.7	11.1	0.0	0.0
Piperacillin-tazobactam	0.0	0.0	0.0	0.0	0.0
Ceftazidime-avibactam	89.5	94.3	77.8	83.3	50.0
Ceftolozane-tazobactam	0.0	2.9	0.0	0.0	0.0
Imipenem-relebactam	68.4	88.6	77.8	83.3	50.0
Meropenem-vaborbactam	68.4	91.4	77.8	83.3	50.0

Figure 2. Most common pathogens stratified by infection type



Other organisms included: *Citrobacter amalonaticus / farmeri* (16), *C. braakii* (1), *C. sedlakii* (1), *Cronobacter sakazakii* (3), *Enterobacter asburiae* (2), *E. cancerogenus* (1), *E. hormaechei* (4), *E. kobei* (2), *E. fergusonii* (1), *E. hermannii* (2), Gram-negative rods in the family Enterobacteriaceae (2), *Hafnia alvei* (16), *H. alvei/ H. paralvei* (1), *Kluyvera ascorbata* (2), *K. georgiana* (1), *Kosakonia cowanii* (1), *Leclercia adecarboxylata* (2), *Lelliottia amnigena* (1), *Pantoea agglomerans* (11), *P. ananatis* (1), *P. anthophila* (1), *P. calida* (1), *P. dispersa* (1), *P. piersonii* (1), *Phytobacter diazotrophicus* (2), *Pluralibacter gergoviae* (8), *Proteus hauseri* (3), *P. penneri* (17), *P. vulgaris* (45), *P. vulgaris group* (39), *Providencia rettgeri* (69), *P. stuartii* (60), *Pseudocitrobacter faecalis* (1), *Rahnella aquatilis* (1), *Raoultella ornithinolytica* (18), *R. planticola* (5), *Serratia fonticola* (1), *S. liquefaciens* (19), *S. liquefaciens complex* (7), *S. odorifera* (2), *S. rubidaea* (1), unspeciated *Citrobacter* (6), unspeciated *Erwinia* (1), unspeciated *Klebsiella* (1), unspeciated *Pantoea* (4), unspeciated *Providencia* (3), unspeciated *Raoultella* (36), unspeciated *Yersinia* (not *Yersinia pestis*) (1), *Yersinia enterocolitica* (1), *Yokenella regensburgei* (1).

Figure 3. Frequency of occurrence of CRE, MDR, and XDR Enterobacterales isolates stratified by infection type (N=11,805)

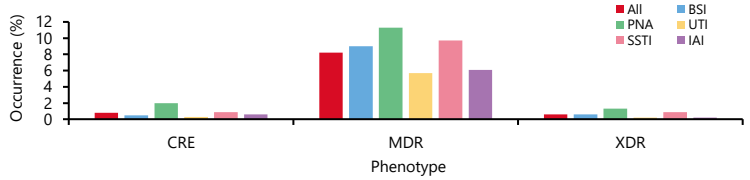
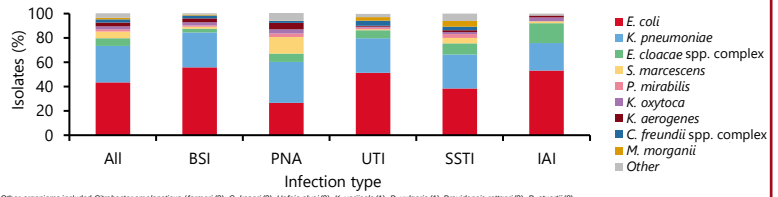


Figure 4. Most common MDR Enterobacterales isolates stratified by infection type



Other organisms included *Citrobacter amalonaticus / farmeri* (3), *C. koseri* (3), *Hafnia alvei* (3), *K. variicola* (1), *P. vulgaris* (1), *Providencia rettgeri* (3), *P. stuartii* (8), *Raoultella ornithinolytica* (3), unspeciated *Citrobacter* (1), unspeciated *Klebsiella* (1), and unspeciated *Raoultella* (8).

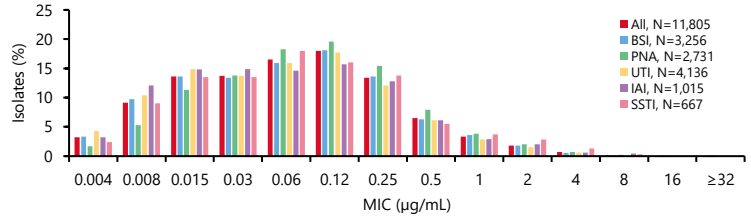



Figure 5. Cefiderocol MIC distribution stratified by infection type