Poster 1360

Activity of Cefiderocol and Comparator Agents Against Difficult-to-Treat Resistant *Pseudomonas aeruginosa* Collected During 2020–2022 as Part of the SENTRY Antimicrobial Surveillance Program

34th ECCMID 2024
Barcelona, Spain
27–30 April, 2024

Contact: Boudewijn L.M. DeJonge
Email: Boudewijn.DeJonge@shionogi.com

Boudewijn L.M. DeJonge,[1] Sean T. Nguyen,[1] Jason J. Bryowsky,[1] Christopher Longshaw,[2] Joshua M. Maher,[3] Rodrigo E. Mendes,[3] Miki Takemura,[4] Yoshinori Yamano[4]

1. Shionogi Inc., Florham Park, NJ, USA; 2. Shionogi B.V., London, UK;
3. JMI Laboratories, North Liberty, IA, USA; 4. Shionogi & Co., Ltd., Osaka, Japan

SHIONOGI

BACKGROUND

- Difficult-to-treat resistant (DTR) *Pseudomonas aeruginosa* shows treatment-limiting resistance to all first-line agents (i.e. β-lactams and fluoroquinolones).
- Cefiderocol is a siderophore-conjugated cephalosporin with a unique mode of entry and excellent activity against resistant *P. aeruginosa*.

OBJECTIVE

We aimed to determine the activity of cefiderocol and comparator agents against DTR *P. aeruginosa*.

METHODS

- Minimum inhibitory concentrations were determined according to Clinical and Laboratory Standards Institute (CLSI) guidelines against 7,310 *P. aeruginosa* isolates, collected in 2020–2022 in Europe (n=3,926) and the USA (n=3,384) as part of the SENTRY program, using broth microdilution with cation-adjusted Mueller–Hinton broth (CAMHB) for comparator agents and iron-depleted CAMHB for cefiderocol.
- Susceptibility was assessed according to European Committee on Antimicrobial Susceptibility Testing (EUCAST), CLSI, and US Food and Drug Administration (FDA) breakpoints.
- DTR *P. aeruginosa* was defined as being non-susceptible, according to CLSI breakpoints, to the β-lactams aztreonam, ceftazidime, cefepime, meropenem, imipenem, and the fluoroquinolones ciprofloxacin and levofloxacin.

RESULTS

- 4.1% (n=299) of *P. aeruginosa* isolates showed the DTR phenotype, with similar percentages for isolates from Europe (4.2%; n=163) and the USA (4.0%; n=136).
- Cefiderocol and colistin were the most active agents against DTR *P. aeruginosa*, while other agents, including novel β-lactam–β-lactamase inhibitor (BL–BLI) combinations, showed much lower activity (Figure 1).
- Metallo-β-lactamases were more frequently encountered among DTR *P. aeruginosa* isolates from Europe than from the USA (Figure 2). This may explain, in part, why DTR *P. aeruginosa* isolates from Europe were more resistant to novel BL–BLI combinations compared with isolates from the USA (Figure 3). In contrast, cefiderocol maintained activity against isolates from both continents.

CONCLUSIONS

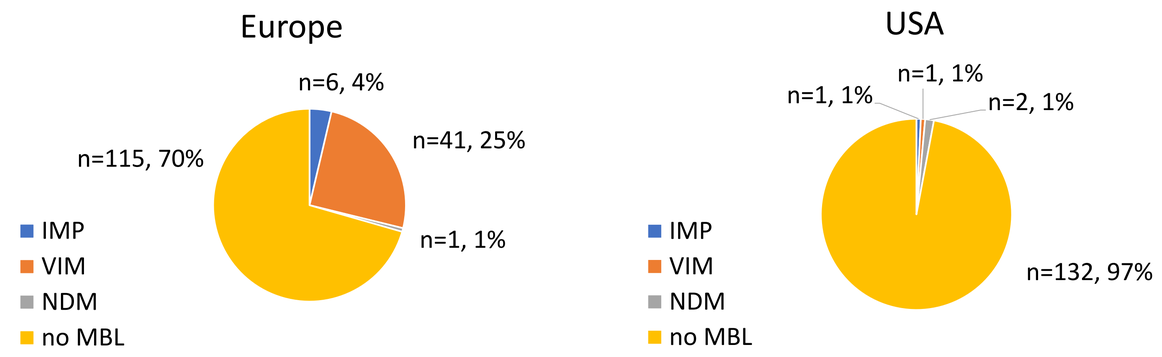
- Contemporary DTR *P. aeruginosa* isolates remained highly susceptible to cefiderocol, while novel BL–BLI combinations exhibited reduced activity against this phenotype.
- Cefiderocol should be considered as an early treatment option for infections known or suspected to be caused by DTR *P. aeruginosa*.

Figure 1: Susceptibility of cefiderocol and comparator agents against difficult-to-treat resistant *P. aeruginosa* (n=299)

- Cefiderocol and colistin showed >90% susceptibility, while much lower percentages were obtained for other agents, including novel BL–BLI combinations.

S, susceptible; I, intermediate; R, resistant; criteria as published by CLSI (2023), EUCAST (2023), and US FDA (2023); for amikacin, only urinary tract infection breakpoints were used.
For systemic infections, aminoglycosides must be used in combination with other active therapy.

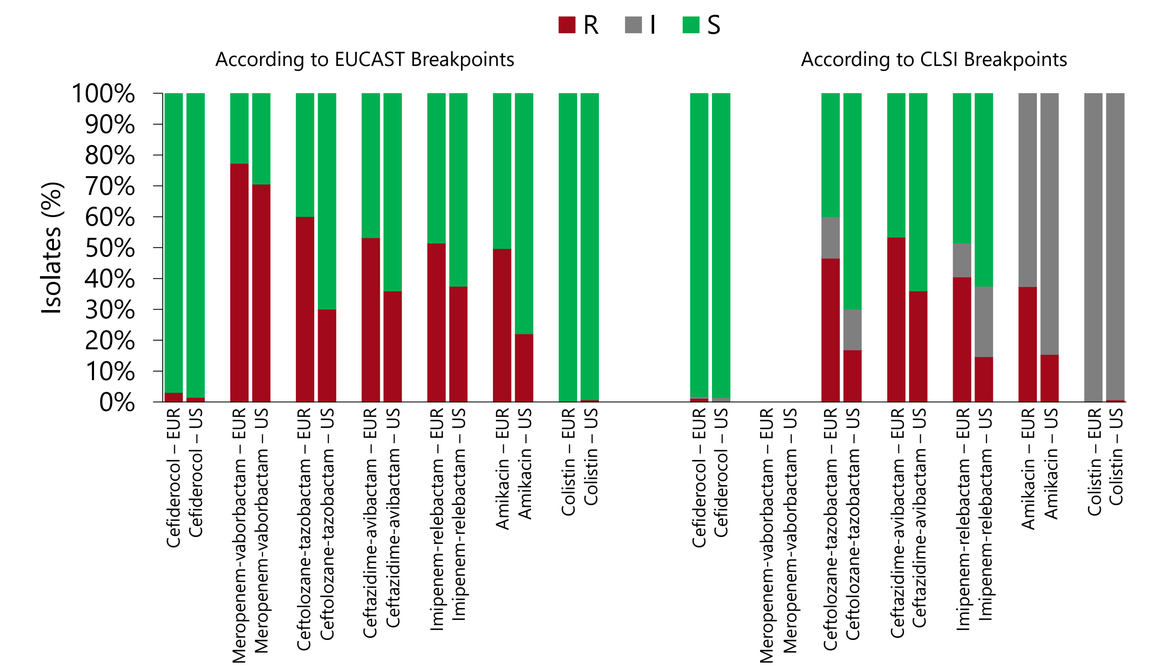
Figure 2: Prevalence of metallo-β-lactamases in difficult-to-treat resistant *P. aeruginosa* from Europe (n=163) and the USA (n=136)



- Metallo-β-lactamases were more frequently encountered in isolates from Europe (29.4%) than in those from the USA (2.9%).

IMP, imipenemase metallo-β-lactamase; MBL, metallo-β-lactamase; NDM, New Delhi metallo-β-lactamase; VIM, Verona integron-encoded metallo-β-lactamase.

Figure 3: Susceptibility of cefiderocol and comparator agents against difficult-to-treat resistant *P. aeruginosa* from Europe (n=163) and USA (n=136) using EUCAST (left) or CLSI (right) breakpoints



- Isolates from Europe were significantly more resistant to all agents compared with isolates from the USA, regardless of which breakpoints were used.
- Resistance for cefiderocol was low for isolates from both continents.

S, susceptible; I, intermediate; R, resistant; criteria as published by CLSI (2023), EUCAST (2023), and US FDA (2023); for amikacin, only urinary tract infection breakpoints were used.
For systemic infections, aminoglycosides must be used in combination with other active therapy.

Acknowledgments

The study was funded by Shionogi. BD, STN, JJB, CL, MT, YY are employees of Shionogi. Editorial support was provided by Highfield, Oxford, UK; this support was funded by Shionogi & Co., Ltd., Osaka, Japan.