In Vitro Activity of Cefiderocol Against Gram-negative Bacteria Isolated from Burn Patients

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- Sean T. Nguyen, Boudewijn L. M. DeJonge, Jason J. Bryowsky, Christopher Longshaw, Miki Takemura, and Yoshinori Yamano are employees of SHIONOGI Group.
- The study was funded by SHIONOGI Group.



Introduction

- Treatment of infections in burn patients can often be complicated by multidrug-resistant bacterial pathogens, which limit the choice of effective antibiotics.
- Cefiderocol, a siderophore cephalosporin, has a unique structure that provides stability against hydrolysis by all classes (A, B, C, and D) of β-lactamases. It has potent *in vitro* activity against isolates resistant to carbapenems.





Study Objectives

- To evaluate the *in vitro* activity of cefiderocol and comparator agents against Gram-negative bacterial isolates collected from burn patients during 2020– 2022 from 26 medical centers in the USA and Europe as part of the SENTRY Antimicrobial Surveillance Program.
 - Minimum inhibitory concentrations (MIC) were determined according to CLSI guidelines using broth microdilution with cation-adjusted Mueller–Hinton broth (CAMHB) for comparator agents and iron-depleted CAMHB for cefiderocol. Susceptibility was assessed per CLSI breakpoints.¹
 - β-lactamase content of *Pseudomonas aeruginosa* and *Acinetobacter* spp. non-susceptible to meropenem and imipenem (Carb-NS) was determined through whole genome sequencing.

¹Enterobacterales, *P. aeruginosa*, *Acinetobacter* spp.: susceptible ≤4 μg/mL; intermediate 8 μg/mL; resistant ≥16 μg/mL;

Stenotrophomonas maltophilia: susceptible ≤1 µg/mL.

Breakpoints are based on a dosage regimen of 2 g every 8 hours, with each dose infused for 3 hours.

Carbapenem-non-susceptible (Carb-NS) phenotype was defined as non-susceptible to meropenem and imipenem.





Distribution of Gram-negative Bacterial Isolates and Infection Sources from Burn Patients



Infection sources (%)



- Pseudomonas aeruginosa
- Acinetobacter baumannii
- Stenotrophomonas
- Acinetobacter courvalinii
- Burkholderia cepacia species complex





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Organism	Count N=151	MIC₅₀ (µg/mL)	MIC ₉₀ (µg/mL)	MIC Range (µg/mL)
Enterobacterales	76	0.12	0.5	0.008 to 4
Carb-NS Enterobacterales	-	-	-	-
P. aeruginosa	40	0.12	0.25	0.03 to 1
Carb-NS P. aeruginosa	12	0.12	0.25	0.03 to 0.25
A. baumannii complex	19	0.12	0.5	0.03 to >64
Carb-NS A. baumannii complex	5	0.25	-	0.12 to >64
S. maltophilia	13	0.06	0.25	0.03 to 0.25
A. courvalinii	2	0.06	-	0.06 to 0.06
<i>B. cepacia</i> species complex	1	-	-	0.12 to 0.12

• 30% of *P. aeruginosa* and 26.3% of *Acinetobacter* spp. were carbapenem-non-susceptible.





Susceptibility of Antimicrobial Agents Against Enterobacterales **Isolates from Burn Patients**



Meropenem/vaborbactam

Pipercillin/tazobactam

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Susceptibility of Antimicrobial Agents Against *P. aeruginosa* Isolates from Burn Patients



* Molecular analyses showed chromosomal AmpC and OXA β -lactamase genes in these isolates, as well as VIM-2 in two isolates.

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Susceptibility of Antimicrobial Agents Against *A. baumannii* Complex Isolates from Burn Patients



Susceptibility of Antimicrobial Agents Against *S. maltophilia* Isolates from Burn Patients







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Conclusions

- Cefiderocol had high *in vitro* activity against contemporary Gramnegative isolates collected from burn patients in United States and European hospitals, including carbapenem-non-susceptible subsets, for which treatment options are limited.
- These data suggest cefiderocol may be a valuable treatment option for burn patients at high risk of serious infections caused by resistant Gram-negative pathogens.



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Thank You

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