

Gram-negative respiratory infections treated with cefiderocol in PROVE, a global retrospective real-world study

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Disclaimer

- The PROVE study is sponsored by Shionogi.
- Stephen Marcella, Sean T. Nguyen, Jay Bryowsky, Stefano Verardi, and Bin Cai are employees of Shionogi.
- Jason Arnold and Maureen Campion are Principal Investigators.
- The study was approved by the central or local Institutional Review Board/ Ethics Committee.
- Patient consents were obtained according to local regulations wherever applicable.

Study design

 PROVE: ongoing, international, retrospective chart review study of the real-world use of cefiderocol in the USA and Europe in patients with Gram-negative bacterial infections (GNBI)

Current analysis included:

- Hospitalized patients with a documented respiratory GNBI who had received their first course of cefiderocol for >72 hours in a regular clinical practice setting
- ✓ Index pathogens were those that prompted the use of cefiderocol
- Outcomes:
 - Clinical resolution of the index GNBI at the end of cefiderocol treatment
 - ✓ Day 14 and Day 30 all-cause mortality from first cefiderocol dose
- Data pull up to December 2, 2022, last hospital day were analyzed

Cefiderocol-treated patients were critically ill with multiple risk factors for CR Gram-negative infections

89.5% of patients had ≥1 risk factor for CR GNBI No risk factors 10.6 Recent travel history

	25				Received cytotoxic chemotherapy	
	3.9				Other bacterial infections	
					Received a transplant within the previous 90 days	
	14.8	ł			Received high-dose corticosteroids	
	14.0	21.5			■ Trauma surgery	
Γ		25.4			History of CR-GNBI	
I		36.3			Received carbapenem within the previous 30 days	5
			51.2		Admitted to hospital in the past 6 months	
				70.7	Recent history of mechanical ventilation	
1	20	10	60	80	100	
0	20	40	60	00	100	
Patients (%)						

Baseline characteristics Age, median (Q1–Q3): 56 (45–65) years Sex: 63.3% male Region: 57.8% from USA Admission from healthcare facilities: 27.7%*

Severity of illness



COVID-19, coronavirus disease 2019; CR, carbapenem resistant; GNBI, Gram-negative bacterial infection;

ICU, intensive care unit; Q, quartile.

*16 patients were included from direct hospital transfers.

Distribution of pathogens in monomicrobial respiratory infections



- 80.9% (207/256) patients had CR infections
- 89.9% (133/148) isolates tested were

cefiderocol susceptible

BSI, bloodstream infection; CR, carbapenem resistant; *no Gram-negative pathogen in respiratory site.

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Top 3 combinations of pathogens in polymicrobial infections:

20% (13/65) *P. aeruginosa* + Enterobacterales
20% (13/65) *A. baumannii* + Enterobacterales
15.4% (10/65) *P. aeruginosa* + *S. maltophilia*

BSI, bloodstream infection; CR, carbapenem resistant; *no Gram-negative pathogen in respiratory site.

Study outcomes by infection site in monomicrobial and polymicrobial infections: clinical cure* rate



Study outcomes by infection site in monomicrobial and polymicrobial infections: Day 14 mortality



Study outcomes by infection site in monomicrobial and polymicrobial infections: Day 30 mortality



Conclusions

- High rates of ICU admission and mechanical ventilation were observed in this critically ill patient population treated with cefiderocol in a real-world setting.
- Patients were at high risk of carbapenem-resistant Gram-negative infections, and difficult-to-treat *P. aeruginosa* was the most frequent pathogen.
 - Polymicrobial infections accounted for approximately 25%.
- Clinical cure rate was impacted by secondary bacteremia.
- Day 14 and Day 30 all-cause mortality rates overall were 16% and 27%, respectively.



THANK YOU FOR YOUR ATTENTION!

Acknowledgment: The authors thank Ray Pecini for his contribution to this analysis.