Comparative Activity of Cefiderocol on Bloodstream Infection Isolates From US ICU patients

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Conflicts of Interest

I have the following conflicts of interest:

Sean T. Nguyen, Boudewijn L.M. DeJonge, Jason J. Bryowsky, Miki Takemura, Yoshinori Yamano are employees of Shionogi.

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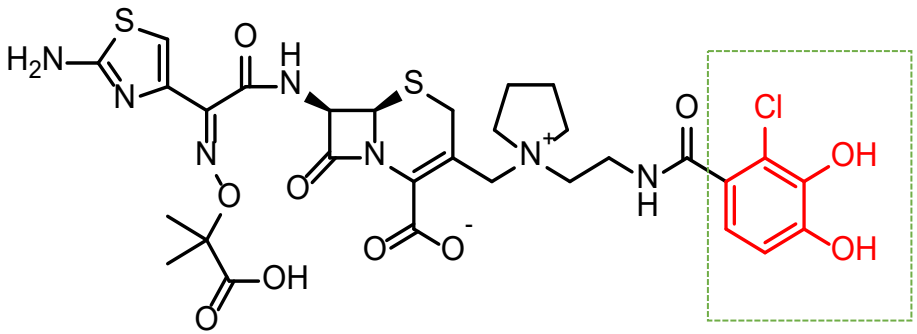
Introduction

- Treatment of bloodstream infections in intensive care unit (ICU) patients can be complicated by antibiotic resistance, which limits the choice of antibiotics.[1]
- Cefiderocol, a siderophore cephalosporin, has a unique structure that provides stability against hydrolysis by all classes (A, B, C, and D) of β-lactamases.[2,3]

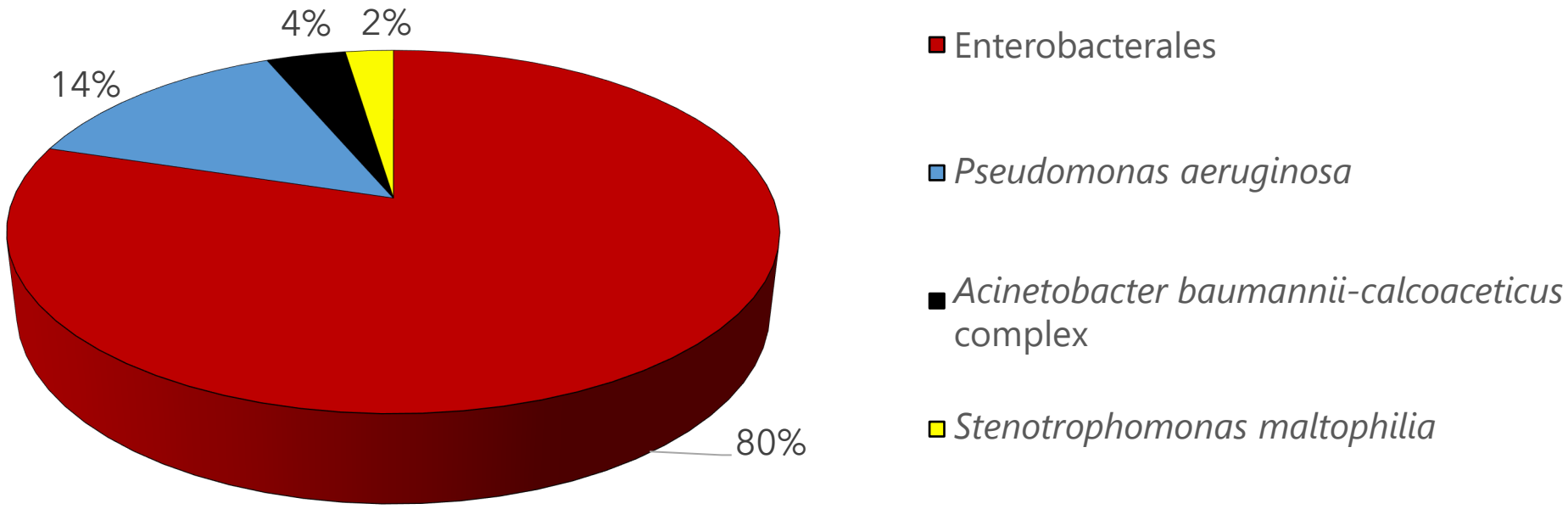


- Cefiderocol has demonstrated potent *in vitro* activity against aerobic Gram-negative pathogens, including isolates resistant to carbapenems.[4]
- Cefiderocol is approved by the US Food and Drug Administration (FDA) for the treatment of complicated urinary tract infections and hospital-acquired/ventilator-associated bacterial pneumonia.[5]

1. Tabah A, et al. Intensive Care Med. 2023;49(2):178-190; 2. Aoki T, et al. Eur J Med Chem. 2018;155:847-868;
3. Sato T, et al. Clin Infect Dis. 2019;69(Suppl 7):S538-S543; 4. Shortridge D, et al. Microbiol Spectr. 2022;10(2):e0271221;
5. Fetroja (cefiderocol). Prescribing information. Shionogi Inc., 2021.

SENTRY Antimicrobial Surveillance Program

- **Study objective**: To evaluate the activity of cefiderocol and comparator agents against aerobic Gram-negative isolates causing bloodstream infection (BSI) in patients hospitalized in intensive care units (ICUs) of US hospitals
- SENTRY 2020–2022: **832 BSI isolates** from 37 US medical center ICUs



In vitro activity of cefiderocol against isolates collected from patients with bloodstream infections in US intensive care units

Organism	Count	MIC_{50} (µg/mL)	MIC_{90} (µg/mL)	MIC Range (µg/mL)
Enterobacterales	664	0.06	0.5	≤0.004 to 16
CarbNS Enterobacterales	6	0.5	NA	0.06 to 4
P. aeruginosa	115	0.12	0.25	≤0.004 to 4
CarbNS *P. aeruginosa*	18	0.12	2	0.015 to 4
A. baumannii complex	33	0.25	2	0.03 to 16
CarbNS *A. baumannii* complex	15	0.25	8	0.06 to 16
S. maltophilia	20	0.06	0.12	0.015 to 1

CarbNS, carbapenem non-susceptible; MIC, minimum inhibitory concentration; NA, not applicable.

Carbapenem non-susceptible phenotype was defined as non-susceptible to meropenem and imipenem.

Cefiderocol susceptibility breakpoints

Antimicrobial susceptibility was assessed according to Clinical and Laboratory Standards Institute (CLSI) and FDA breakpoints.

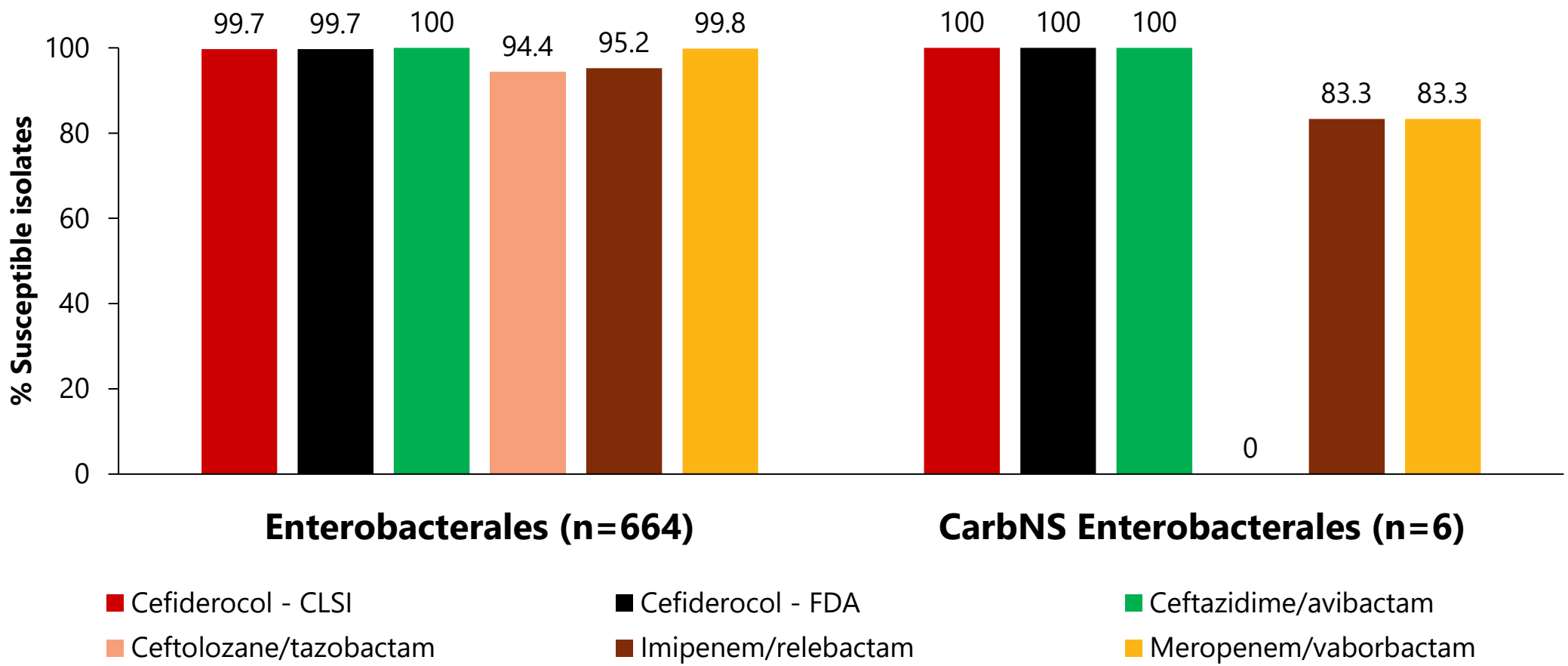
CLSI Breakpoints	Minimum Inhibitory Concentrations (µg/mL)		
	Susceptible	Intermediate	Resistant
Enterobacterales	≤4	8	≥16
P. aeruginosa	≤4	8	≥16
A. baumannii complex	≤4	8	≥16
S. maltophilia	≤1	-	-

FDA Breakpoints	Minimum Inhibitory Concentrations (µg/mL)		
	Susceptible	Intermediate	Resistant
Enterobacterales	≤4	8	≥16
P. aeruginosa	≤1	2	≥4
A. baumannii complex	≤1	2	≥4

- Breakpoints are based on a dosage regimen of 2 g every 8 hours administered over 3 hours.

1. US FDA. Antibacterial Susceptibility Test Interpretive Criteria. 2021. https://www.fda.gov/drugs/development-resources/cefiderocol-injection. Accessed May 11, 2023.
2. CLSI. Performance Standards for Antimicrobial Susceptibility Testing, 33rd Edition. M100. 2023.

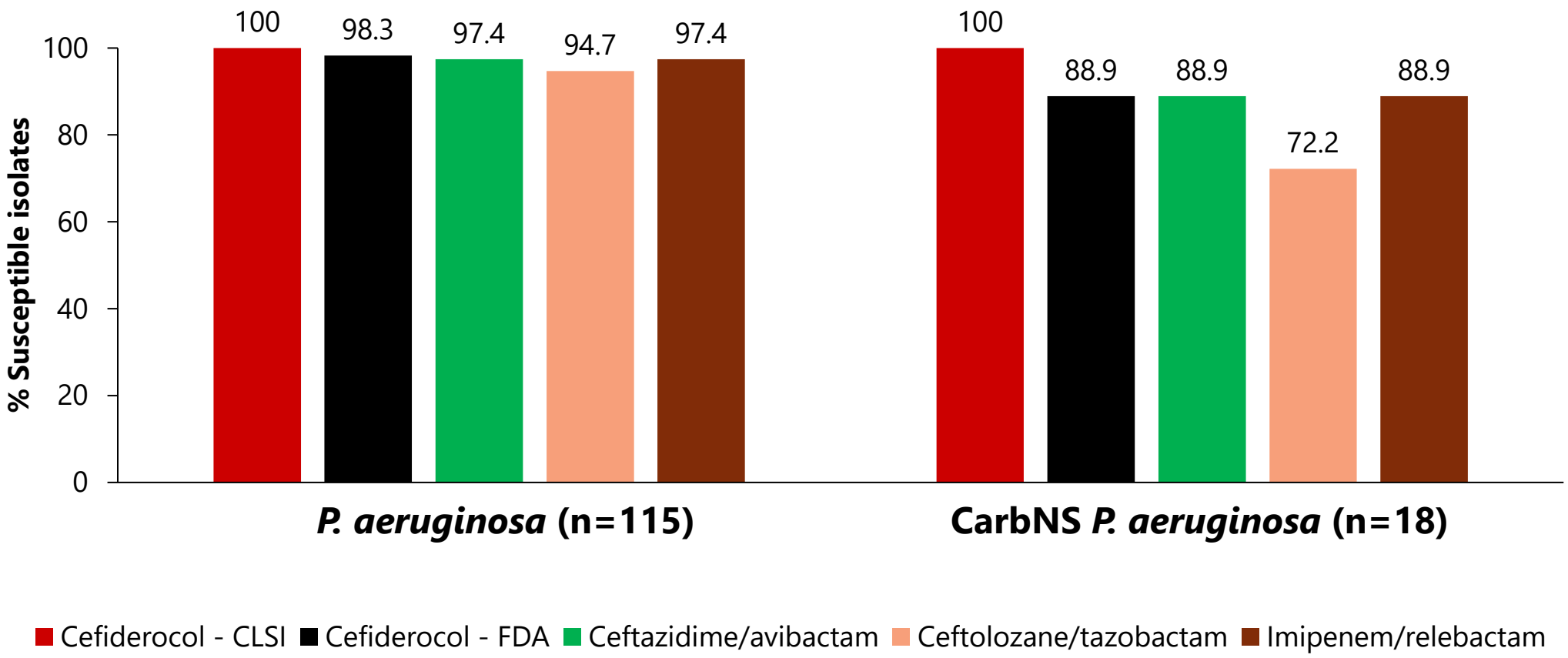
Susceptibility of antimicrobial agents against Enterobacterales isolates from bloodstream infections



- 0.9% CarbNS Enterobacterales

CarbNS, carbapenem non-susceptible.

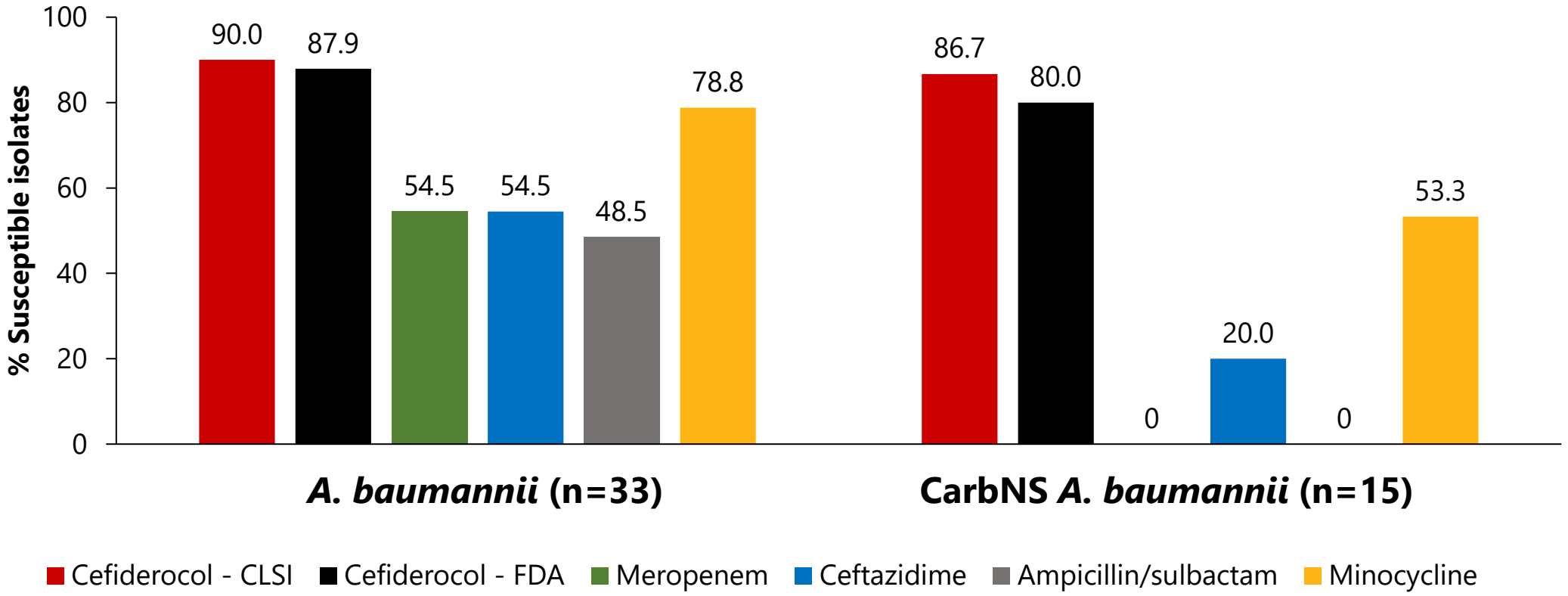
Susceptibility of antimicrobial agents against *P. aeruginosa* isolates from bloodstream infections



CarbNS, carbapenem non-susceptible.

- 15.7% CarbNS *P. aeruginosa*

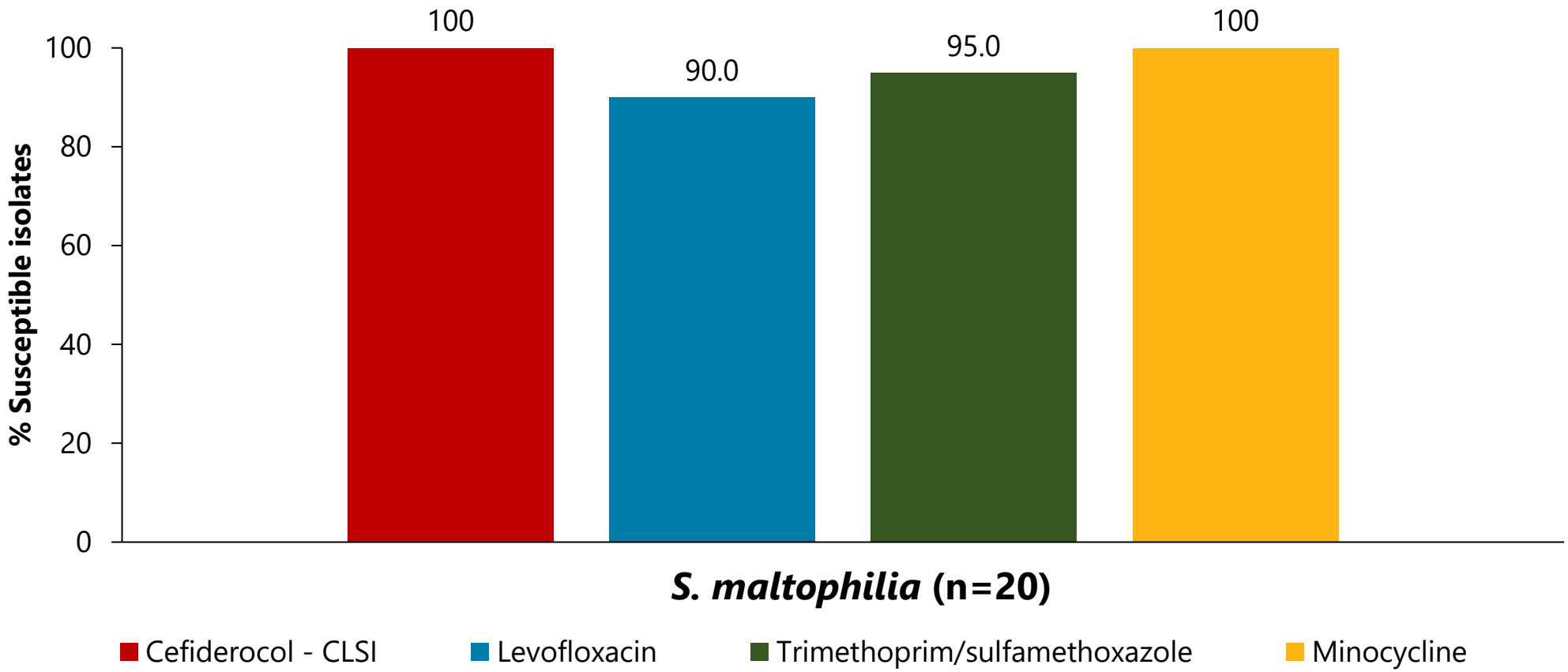
Susceptibility of antimicrobial agents against *A. baumannii* complex isolates from bloodstream infections



- 45.5% CarbNS *A. baumannii* complex

CarbNS, carbapenem non-susceptible.

Susceptibility of antimicrobial agents against *S. maltophilia* isolates from bloodstream infections



Conclusions

- Against bloodstream isolates collected from ICU patients from US hospitals, cefiderocol was a highly active agent, with >90% susceptibility against Enterobacterales, *P. aeruginosa*, *A. baumannii-calcoaceticus* complex, and *S. maltophilia*.
  - Cefiderocol remained highly active against carbapenem non-susceptible isolates, for which treatment options are limited.

- Cefiderocol represents a potential option for empiric antimicrobial therapy in ICU patients in the USA for the treatment of bloodstream infections suspected of being caused by carbapenem-resistant Gram-negative pathogens.

Thank you for your time!

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