Comparative Activity of Newer β-Lactam/β-Lactamase Inhibitor Combinations against *Pseudomonas aeruginosa* from Patients in ICU of US Medical Centres in 2021

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Objectives

- To evaluate the susceptibility of contemporary *P. aeruginosa* isolates from ICU and non-ICU patients to 4 new β-lactamase inhibitor combinations (BLICs): ceftazidime-avibactam (CAZ-AVI), ceftolozane-tazobactam (C-T), meropenem-vaborbactam (MEM-VAB), and imipenem-relebactam (IMI-REL).

Materials and Methods

- The isolate number was updated since the submission of the abstract as additional isolates were tested.
- 1,423 isolates (497 from ICU and 926 from non-ICU patients) were consecutively collected in 59 US medical centres in 2021.
- Isolates were tested by reference broth microdilution (CLSI).
- EUCAST interpretive criteria were applied.
- Pneumonia was the predominant infection among ICU (80.1%) and non-ICU patients (34.0%).

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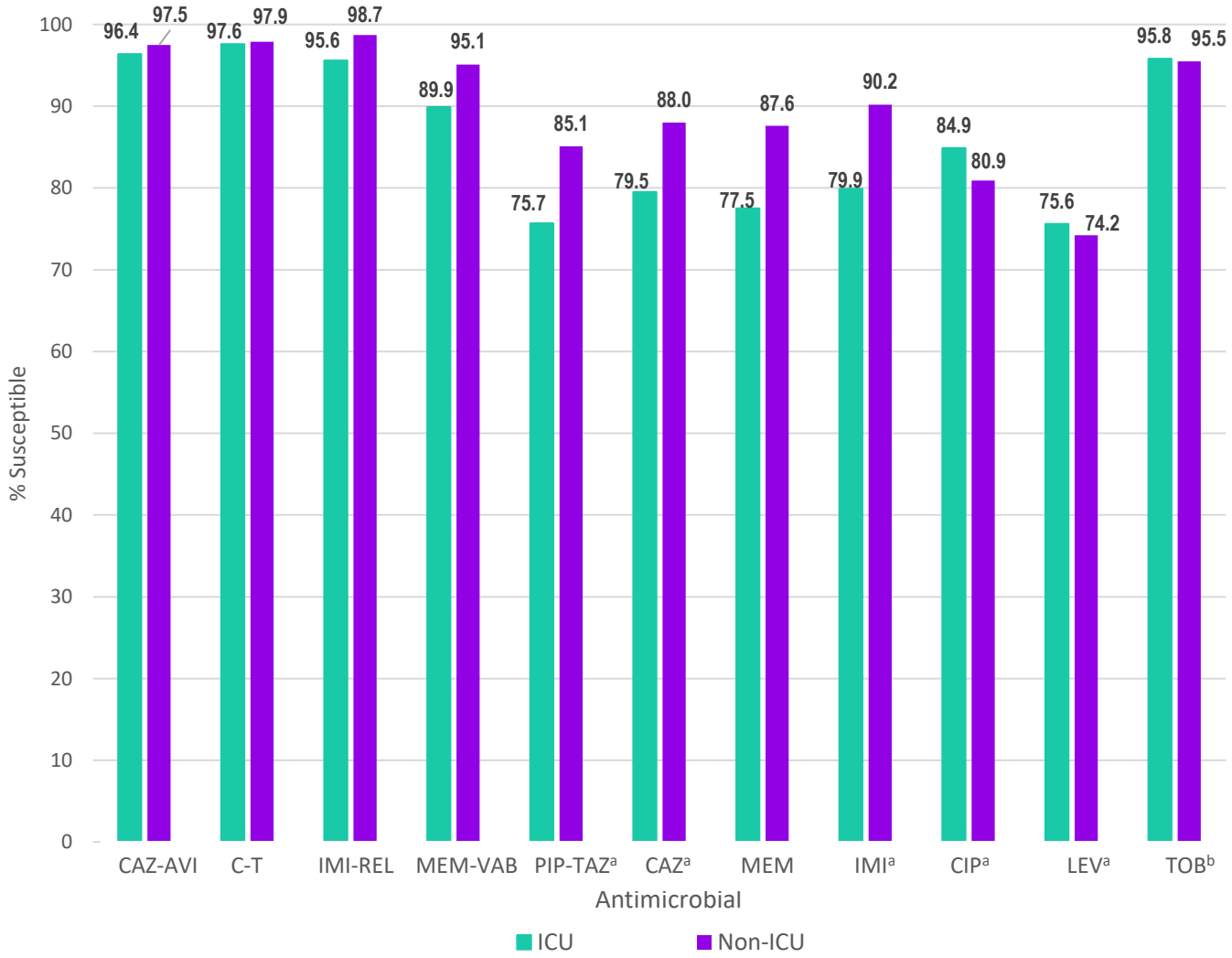
Results

Figure 1. Antimicrobial susceptibility of *P. aeruginosa* from ICU and non-ICU patients

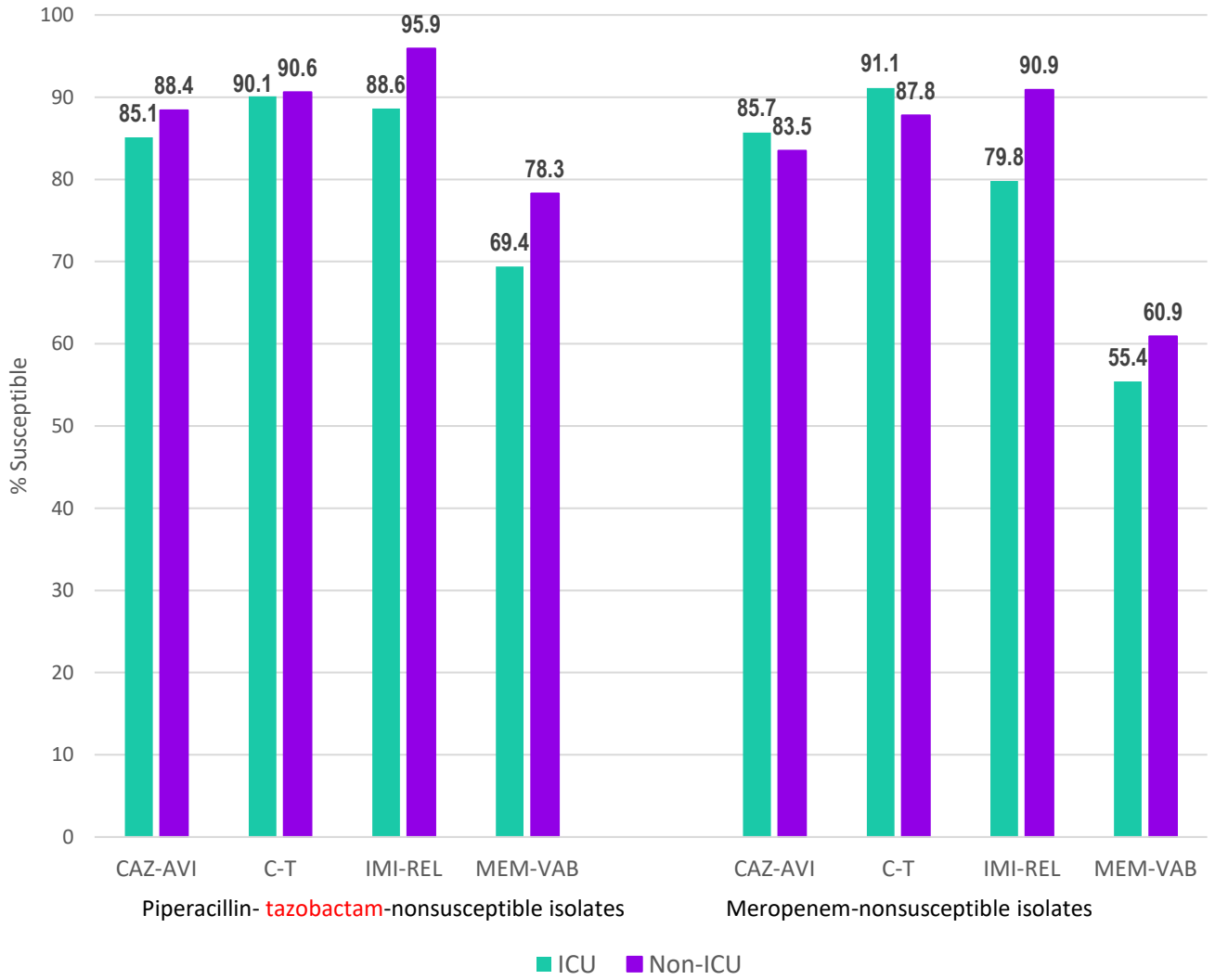


- CAZ-AVI, C-T, and IMI-REL exhibited similar activity and broad coverage against ICU (95.6-97.6%S) and non-ICU (97.5-98.7%S) isolates.
- MEM-VAB was slightly less active than the other 3 BLIs against ICU (89.9%S) isolates.
- The most active comparator agents were colistin, amikacin (not shown), and tobramycin (TOB).
- Susceptibility rates for the BLICs, ceftazidime (CAZ), cefepime (not shown), meropenem (MEM), and imipenem (IMI) were lower among isolates from ICU compared to non-ICU patients.
- In contrast, susceptibility to ciprofloxacin (CIP), levofloxacin (LEV), and amikacin (not shown) were slightly higher among isolates from ICU patients.

[a] Susceptible, increased exposure.
[b] Using UTI breakpoints.

Results

Figure 2. Activity of the 4 BLICs against PIP-TAZ-NS and MEM-NS isolates



- CAZ-AVI, C-T, and IMI-REL retained potent activity against *P. aeruginosa* isolates non-susceptible to PIP-TAZ or meropenem.
- MEM-VAB was slightly less active than the other 3 BLICs against these resistant subsets.
- MDR and XDR phenotypes were more common among ICU than non-ICU isolates.

Table 1. Frequency of MDR and XDR phenotypes

Phenotype	ICU	Non-ICU
MDR	15.3%	9.3%
XDR	7.1%	4.1%

Results

Table 2. Cross Resistance Among New BLIs

Resistance phenotype (no.)	% Susceptible per EUCAST (ICU plus non-ICU)			
	CAZ-AVI	C-T	IMI-REL	MEM-VAB
CAZ-AVI-R-R (41)	--	51.2	69.7	29.3
C-T-R (31)	35.5	--	75.0	51.6
IMI-REL-R (27)	63.0	77.8	--	11.1
MEM-VAB-R (95)	69.5	15.8	70.7	--

- Rates of cross-resistance among the 4 new BLICs varied markedly.
- CAZ-AVI remained active against approximately two-thirds of isolates resistant to IMI-REL or MEM-VAB.
- Similarly, IMI-REL remained active against ≥69% of isolates resistant to any of the other 3 new BLICs.

Conclusions

- The BLICs CAZ-AVI, C-T, and IMI-REL were highly active and exhibited similar coverage against *P. aeruginosa* from both ICU and non-ICU patients.
- These BLICs represent valuable new therapeutic options for the treatment of *P. aeruginosa* infections.
- Resistance rates to the β-lactams were generally higher among ICU than non-ICU isolates.