# Frequency, Antimicrobial Susceptibility, and Molecular Characterization of **Carbapenem-Resistant Enterobacterales** Stratified by United States Census **Divisions: Results from the INFORM Program (2018–2022)**

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# CONCLUSIONS



ATM-AVI showed potent activity against CRE, including MBL producers, from all US Census Divisions.



Resistance to CAZ-AVI and MEM-VAB among CRE was observed in the New England, Middle Atlantic, and Mountain Census Divisions due to increasing occurrence of isolates producing MBL and/or OXA-48-like.

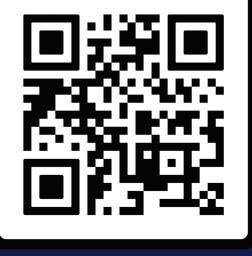
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### Funding

This study was supported by AbbVie. Helio S. Sader, John H. Kimbrough, Timothy Doyle, Cecilia Carvalhaes, and Mariana Castanheira are employees of JMI Laboratories, which was paid consultant to AbbVie in connection with the development of this poster.

### Acknowledgements

The authors thank all the participant centers for their work in providing isolates.

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## INTRODUCTION

- demonstrated a broad spectrum of activity against carbapenem-resistant Enterobacterales (CRE) from US hospitals, but resistance may emerge with the increasing use of these compounds.
- Aztreonam-avibactam (ATM-AVI) has shown potent activity against CRE, including MBL producers, and is under clinical development.
- We evaluated the activity of ATM-AVI and comparators against CREs from US hospitals.

### METHODS

- 45,497 Enterobacterales isolates were consecutively collected from 79 US medical centers (36 states) in 2018–2022 and susceptibility tested by CLSI broth microdilution.
- ATM-AVI was tested with AVI at a fixed 4 mg/L and a susceptible breakpoint of  $\leq 8$  mg/L was applied for comparison.
- Results were stratified by US Census Divisions (Table1 and Figure 1).
- CRE isolates were screened for carbapenemase (CPE) by whole genome sequencing.

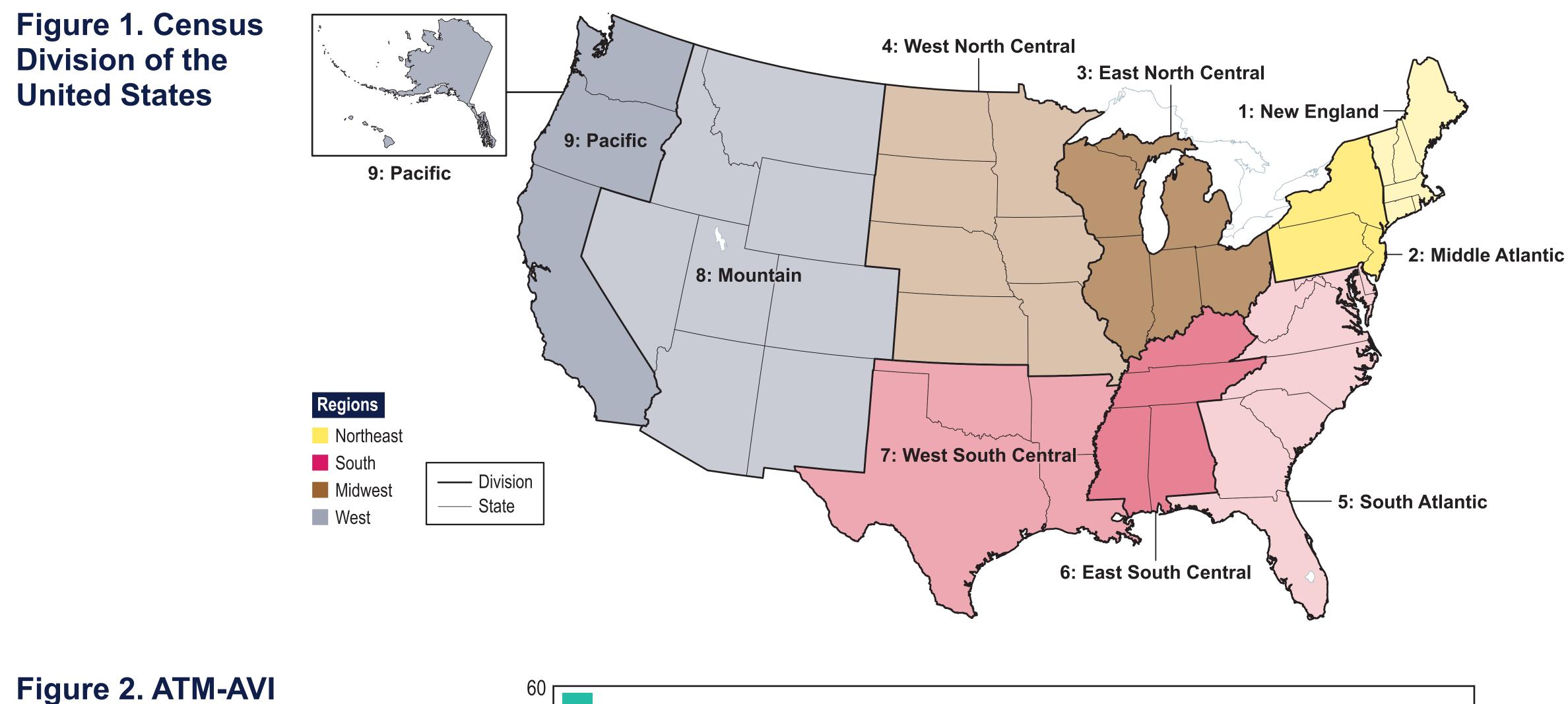
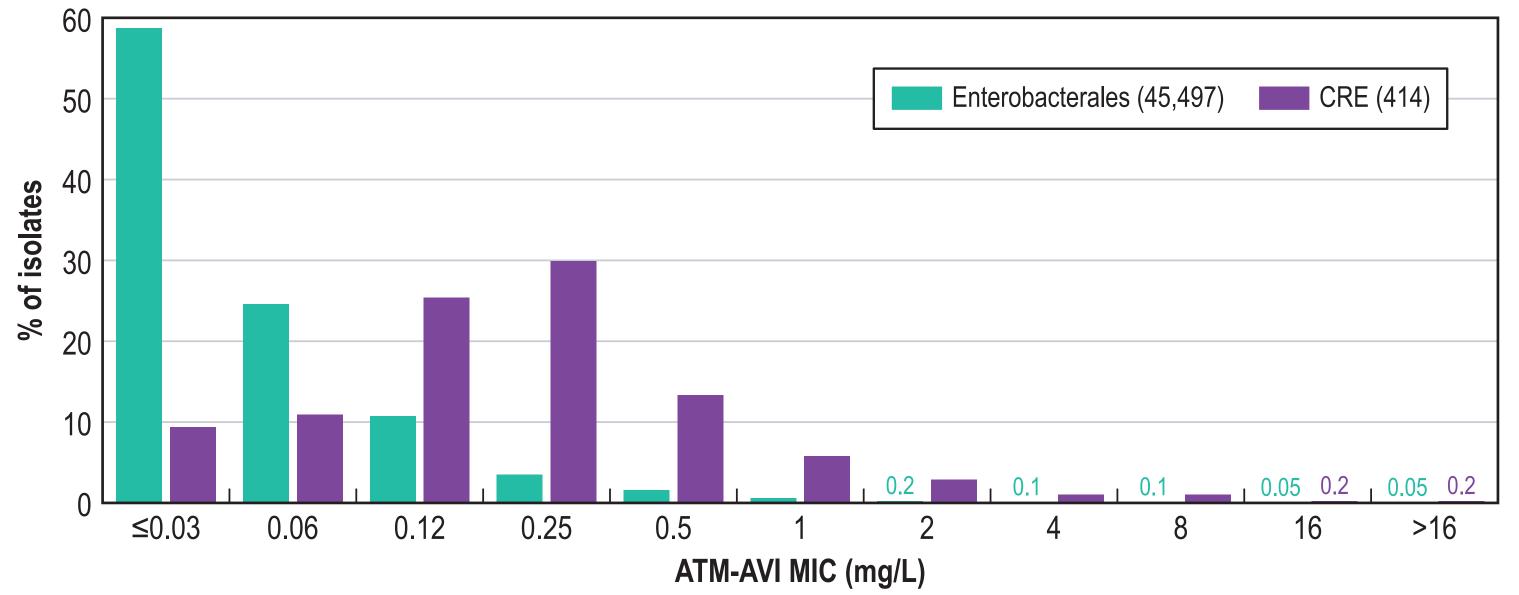


Figure 2. ATM-AVI **MIC distributions for Enterobacterales and CRE** isolates from US medical centers (2018–2022)



### Table 2. Antimicrobial susceptibility of Enterobacterales stratified by US Census Division (2018–2022)

Antimicrobial agent	% Susceptible per Census Division (no. of isolates)									
	1 (3,294)	2 (7,077)	3 (7,799)	4 (4,216)	5 (6,160)	6 (3,347)	7 (4,444)	8 (4,059)	9 (5,101)	All (45,497)
Ceftazidime-avibactam	>99.9	99.5	>99.9	100.0	99.9	99.9	99.9	99.7	99.9	99.9
Meropenem-vaborbactam	>99.9	99.4	>99.9	100.0	>99.9	100.0	99.7	99.7	99.9	99.8
Imipenem-relebactam <sup>b</sup>	93.7	91.7	92.6	93.9	94.3	92.6	92.5	94.4	93.4	93.1
Ceftolozane-tazobactam	96.5	91.5	95.8	96.2	95.0	95.2	94.1	94.1	94.6	94.6
Piperacillin-tazobactam	94.7	0.88	93.6	94.8	92.7	93.5	90.4	92.5	92.7	92.3
Ceftriaxone	87.8	74.3	87.2	88.7	84.8	84.1	80.3	83.9	82.4	83.3
Ceftazidime	90.2	79.9	90.1	91.7	87.8	88.0	84.8	87.4	86.3	87.0
Cefepime	92.8	82.7	93.4	94.8	91.2	91.0	87.4	91.2	89.9	90.2
Meropenem	99.7	97.5	99.4	99.8	99.5	99.5	98.4	99.3	99.0	99.0
Imipenem <sup>b</sup>	92.5	88.4	90.1	92.0	91.9	90.2	90.5	91.4	90.1	90.6
Levofloxacin	85.0	76.1	84.9	87.2	82.4	81.6	76.9	85.5	84.2	82.4
Gentamicin	93.1	88.5	93.1	94.2	91.8	92.7	89.5	92.7	91.4	91.7
Amikacin	95.7	93.2	95.4	96.0	95.4	95.6	93.1	95.8	95.5	95.0
Tigecycline	96.5	94.2	94.8	96.5	95.6	94.9	94.7	95.9	94.8	95.2

a % inhibited at ≤8 mg/L b All Enterobacterales species were included in the analysis, but CLSI excludes Morganella, Proteus, and Providencia species.

• Recently approved β-lactamase inhibitor combinations (BLIs), such as ceftazidime-avibactam (CAZ-AVI) and meropenem-vaborbactam (MEM-VAB), have

 Table 1. Census divisions of the United States

#### **Division designation** Division no. New England Middle Atlantic East North Central West North Central South Atlantic East South Central

Mountain

Pacific

West South Central

## RESULTS

- respectively (Table 2).

- ≤8 mg/L).

- England (Figure 5).

### Figure 3. Frequency of CRE stratified by US Census **Division (2018–2022)**

Figure 4. Activities of aztreonam-avibactam (ATM-AVI), ceftazidime-avibactam (CAZ-AVI), meropenemvaborbactam (MEM-VAB) and imipenem-relebactam (IMI-REL) against CRE isolates from US medical centers (2018–2022)

### **Figure 5. Frequency of** carbapenemases (CPE) among CRE isolates stratified by US Census Divisions

• ATM-AVI inhibited >99.9% of Enterobacterales at ≤4 mg/L and only 4 isolates (<0.01%) showed ATM-AVI MICs >8 mg/L (Table 2 and Figure 2). • CAZ-AVI (MIC<sub>50/90</sub>, 0.12/0.25 mg/L) and MEM-VAB (MIC<sub>50/90</sub>, 0.03/0.03 mg/L) were active against 99.9% and 99.8% of Enterobacterales isolates,

• CRE rates varied from 0.1% (West North Central) to 2.4% (Middle Atlantic; Figure 3).

• ATM-AVI was active (MIC ≤8 mg/L) against 99.5% (412/414) of CREs, whereas susceptibility to CAZ-AVI and MEM-VAB were lowest in the Mountain division (67.7% and 74.2%, respectively) and highest (100.0%) in West North Central (Figure 4).

• ATM-AVI retained activity against Enterobacterales non-susceptible to CAZ-AVI and/or MEM-VAB (n=73; MIC<sub>50/90</sub>, 0.25/2 mg/L; 98.6% inhibited at

• KPC was the most common CPE (65.0% of CREs), followed by NDM (8.2%) and OXA-48–like (3.6%; Figure 5).

• An MBL gene was detected in 9.7% of CREs and a CPE gene was not identified in 20.8% of CREs (Figure 5).

• The occurrence of KPC among CREs varied from 14.3% (1/7; New England) to 77.8% (14/18; East South Central); whereas the frequency of metalloβ-lactamases (MBLs) ranged from <3.0% (South Atlantic, East North Central, and Pacific) to 19.4% (6/31) in Mountain region and 42.9% (3/7) in New

