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# Aztreonam-avibactam activity against Enterobacterales from United States medical centers: Summary of 5 years of surveillance prior to approval for clinical use (2020–2024)

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## CONCLUSIONS

ATM-AVI demonstrated almost complete activity against Enterobacterales and retained potent activity against CRE, including MBL producers.

Importantly, ATM-AVI activity was not adversely affected by clinically relevant carbapenemases or resistance to agents used to treat multidrug-resistant Enterobacterales.

The activities of CAZ-AVI, MEM-VAB, and IMI-REL were compromised by the increased occurrence of MBL producers among CRE isolates from US medical centers.

These results provide a valuable benchmark for monitoring the *in vitro* activity of ATM-AVI after regulatory approval and emphasize the importance of comprehensive surveillance programs to monitor the emergence of resistance mechanisms to newly approved antimicrobial agents.

## INTRODUCTION

- Aztreonam-avibactam (ATM-AVI) was approved by the United States (US) Food and Drug Administration (FDA) to treat intra-abdominal infections in February 2025.
- We evaluated the *in vitro* activity of ATM-AVI against Enterobacterales from US hospitals during the 5-year period prior to its approval for clinical use.

## METHODS

- A total of 42,225 isolates (1/patient) were consecutively collected in 2020–2024 from 85 US medical centers.
- Only bacterial isolates determined to be significant by local criteria as the reported probable cause of infection were included in the study.
- Isolates were susceptibility tested by Clinical and Laboratory Standards Institute (CLSI) M07 broth microdilution methods at a monitoring laboratory.
- Susceptibility results were stratified by year.
- Carbapenem-resistant Enterobacterales (CRE; *n*=406 [1.0%]) and isolates with elevated ATM-AVI MICs (>4 mg/L) were molecularly characterized.

## RESULTS

- ATM-AVI was active against 99.9% of Enterobacterales and exhibited potent activity against CRE ($MIC_{50/90}$, 0.25/1 mg/L; 97.0% susceptible [S]; Table 1).
- Ceftazidime-avibactam (CAZ-AVI), meropenem-vaborbactam (MEM-VAB), and imipenem-relebactam (IMI-REL) were very active against Enterobacterales overall (93.8–99.7% S) but showed moderate activity against CRE (67.5–76.1% S; Table 1).
- CRE susceptibility to CAZ-AVI decreased from 89.2% in 2020 to 69.1% in 2024 (Table 1 and Figure 1).
- CRE susceptibility to MEM-VAB decreased from 83.1% in 2020 to 66.0% in 2024 (Table 1 and Figure 1).
- Cefiderocol ($MIC_{50/90}$, 1/4 mg/L) was active against 94.1% of CREs (Table 1).
- The most common carbapenemases (CBase) among CREs were KPC (52.7% of CREs), NDM (21.2%), and OXA-48-like (4.4%).
- A CBase was not identified in 20.7% of CREs.
- The frequency of KPC decreased from 67.5% in 2020 to 39.4% in 2024 (Figure 2).
- The frequency of MBL ranged from 12.0% in 2020 to 43.8% in 2023 (23.4% overall; Figure 2).
- ATM-AVI, CAZ-AVI, MEM-VAB, IMI-REL, and cefiderocol were very active (≥98.1% S) against KPC producers (Table 2).
- Only ATM-AVI (97.9% S) and cefiderocol (84.2% S) showed good activity against MBL producers (Table 2).
- Only 27 isolates (<0.1%) had ATM-AVI MIC >4 mg/L; 55.6% and 66.7% of them were meropenem-S and CAZ-AVI-S, respectively.
- Decreased susceptibility to ATM-AVI was mainly due to PBP3 alterations and production of CMY and/or CTX-M among *E. coli*, and porin alterations plus β-lactamase production in *E. cloacae* and *Klebsiella* spp.

**Table 1. Yearly susceptibility of CRE isolates**

| Antimicrobial agent | % Susceptible per CLSI and/or US FDA (no. of isolates) | | | | | |
|---|---|---|---|---|---|---|
| | 2020 (83) | 2021 (98) | 2022 (67) | 2023 (64) | 2024 (94) | All years (406) |
| Aztreonam-avibactam | 100.0 | 96.9 | 97.0 | 100.0 | 92.6 | 97.0 |
| Ceftazidime-avibactam | 89.2 | 78.6 | 83.6 | 57.8 | 69.1 | 76.1 |
| Meropenem-vaborbactam | 83.1 | 76.5 | 80.6 | 53.1 | 66.0 | 72.4 |
| Imipenem-relebactam | 77.1 | 70.4 | 74.6 | 48.4 | 63.8 | 67.5 |
| Cefiderocol | 92.8 | 92.9 | 95.5 | 93.8 | 95.7 | 94.1 |
| Amikacin | 55.4 | 59.2 | 79.1 | 64.1 | 70.2 | 65.0 |
| Gentamicin | 51.8 | 55.1 | 76.1 | 70.3 | 63.8 | 62.3 |
| Levofloxacin | 25.3 | 28.6 | 41.8 | 31.2 | 34.0 | 31.8 |
| Tigecycline | 94.0 | 91.8 | 98.5 | 96.9 | 97.9 | 95.6 |
| Colistin | 84.3 | 84.7 | 83.6 | 78.1 | 87.2 | 84.0 |

**Table 2. Antimicrobial susceptibility of CRE isolates stratified by carbapenemase type**

| Antimicrobial agent | % Susceptible per CLSI and/or US FDA (no. of isolates) | | | | |
|---|---|---|---|---|---|
| | All CRE (406)[a] | KPC producers (206)[a] | MBL producers (95) | Other carbapenemases (21)[a,b] | No carbapenemase identified (84) |
| Aztreonam-avibactam | 97.0 | 100.0 | 97.9 | 95.2 | 89.3 |
| Ceftazidime-avibactam | 76.1 | 99.5 | 6.3 | 95.2 | 92.9 |
| Meropenem-vaborbactam | 72.4 | 99.5 | 10.5 | 38.1 | 84.5 |
| Imipenem-relebactam | 67.5 | 98.1 | 2.1 | 4.8 | 82.1 |
| Cefiderocol | 94.1 | 99.0 | 84.2 | 95.2 | 92.9 |
| Amikacin | 65.0 | 60.7 | 55.8 | 57.1 | 88.1 |
| Gentamicin | 62.3 | 51.9 | 66.3 | 61.9 | 83.3 |
| Levofloxacin | 31.8 | 27.2 | 18.9 | 42.9 | 54.8 |
| Tigecycline | 95.6 | 97.6 | 94.7 | 85.7 | 94.0 |
| Colistin | 84.0 | 83.5 | 86.3 | 61.9 | 88.1 |

[a] Excludes MBL co-producers
[b] Includes isolates with OXA-48-like (13), SME (7), or IMI (1).

**Figure 1. Yearly susceptibility of CRE isolates**

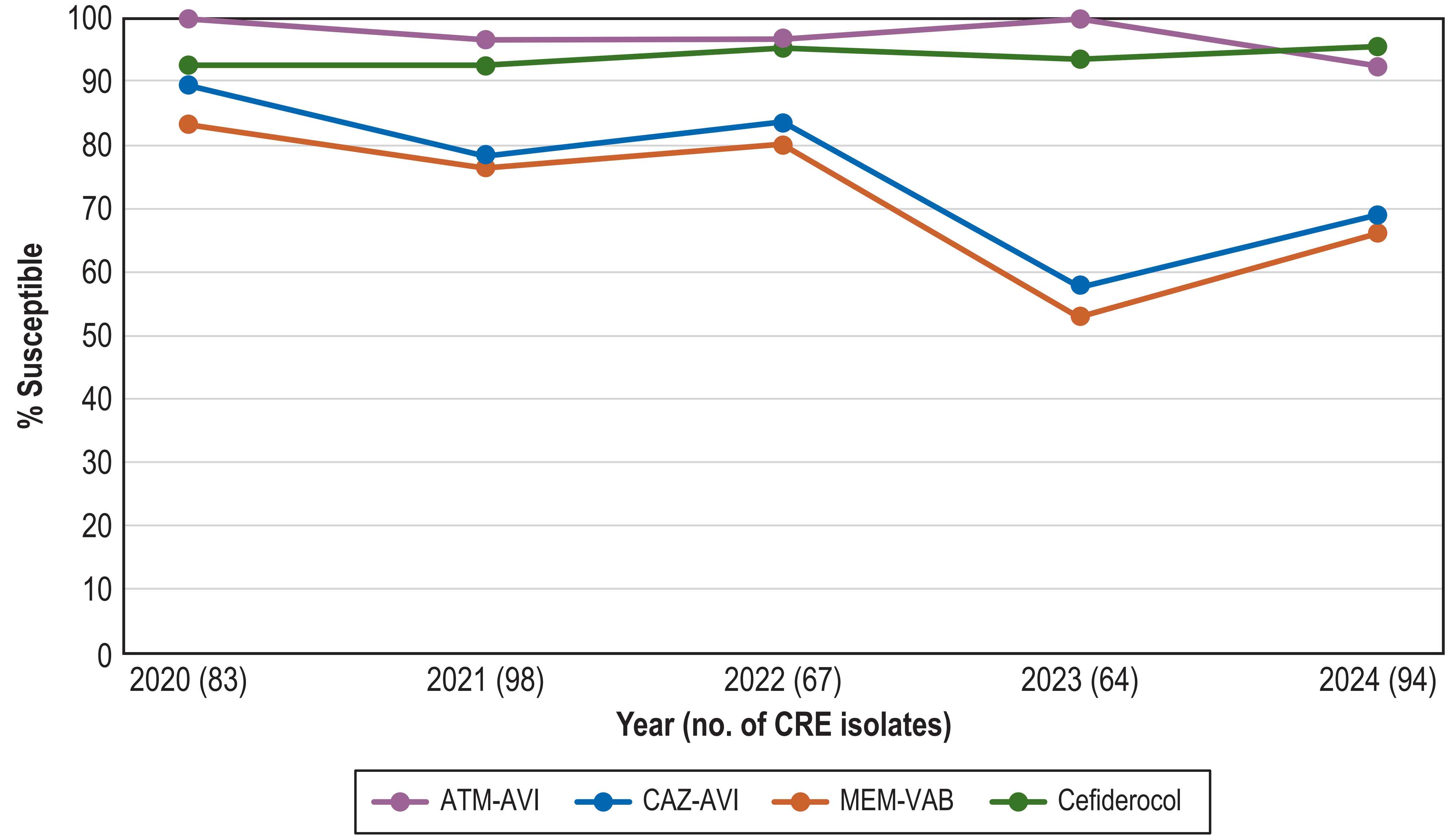
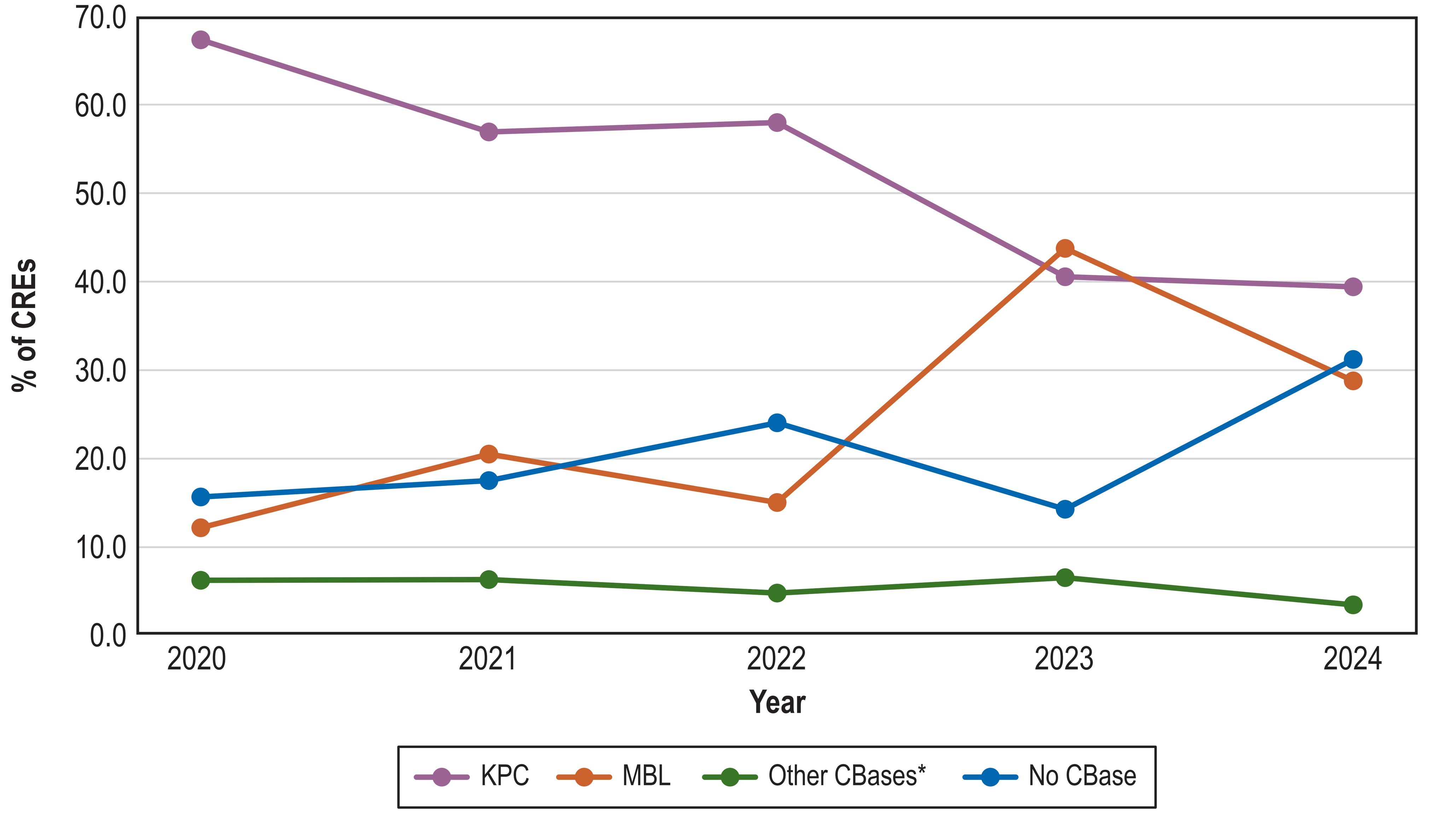

100
90
80
70
60
50
40
30
20
10
0
% Susceptible
2020 (83)
2021 (98)
2022 (67)
2023 (64)
2024 (94)
Year (no. of CRE isolates)
ATM-AVI
CAZ-AVI
MEM-VAB
Cefiderocol

**Figure 2. Yearly frequency of carbapenemases (CBases) among CREs**


70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
% of CREs
2020
2021
2022
2023
2024
Year
KPC
MBL
Other CBases*
No CBase

* Includes isolates with OXA-48-like (13), SME (7), or IMI (1); excludes MBL co-producers.

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