

Introduction

Ceftazidime-avibactam (CAZ-AVI) is a therapeutic agent consisting of a third-generation cephalosporin ceftazidime and a diazabicyclooctane β -lactamase inhibitor avibactam that inhibits Class A, C, and some Class D β -lactamases produced by Gram-negative bacteria. The *in vitro* activities of CAZ-AVI and comparator agents were evaluated against clinical isolates of Enterobacterales collected from lower respiratory tract (LRT) infections in the Asia/Pacific (APAC) region as part of the ATLAS global surveillance program from 2020-2024 [1].

Materials & Methods

- 4,363 Enterobacterales isolates from the LRT were collected from 43 sites in 10 countries: Australia, Hong Kong, India (excluding 2024 isolates not available for molecular characterization), Japan, Malaysia, New Zealand, Philippines, South Korea, Taiwan, and Thailand. These were compared to 14,128 isolates collected from 170 sites in 46 countries in the rest of the world, excluding North America (RoW).
- Antimicrobial susceptibility was determined by broth microdilution according to CLSI guidelines [2] and interpreted using CLSI 2026 breakpoints [3] while FDA breakpoints were used for tigecycline [4].
- Meropenem-nonsusceptible (MEM-NS) isolates were screened for β -lactamases by PCR and Sanger sequencing (2020-2023) or WGS (2024). PCR+Sanger sequencing was performed as previously described [5]. WGS was by Oxford Nanopore sequencing (Promethion R10 flow cells) and genes encoding β -lactamases were detected using AbriTAMR [6] which uses the AMRFinderPlus database [7].

Results Summary

- K. pneumoniae* was the most commonly identified organism among MEM-NS isolates for both APAC and RoW (Figure 1a and Figure 1b).
- E. coli* comprised 16% of MEM-NS+metallo- β -lactamase-positive (MBL-POS) Enterobacterales isolates in APAC compared to 3% in RoW (Figure 1a and Figure 1b).
- Carbapenem-resistant Enterobacterales (CRE) represented the 16.0% of all collected isolates from APAC and the 9.1% of those from RoW.
- More NDM, OXA-48-like, and NDM+OXA-48-like carriage was identified among CRE in APAC compared to RoW. On the other hand, more KPC carriage was observed in RoW (Figure 3).
- CAZ-AVI was active against isolates from APAC (90% susceptible) and RoW (96.3% susceptible); fewer isolates were susceptible to comparator agents except against tigecycline (Table 1).
- Of MBL-negative isolates carrying KPC or OXA-48-like carbapenemases, 97.0-98.4% were susceptible to ceftazidime-avibactam regardless of region of collection (Table 1).

Conclusion

Ceftazidime-avibactam demonstrated potent *in vitro* activity against lower respiratory tract Enterobacterales isolates, including those that produced KPC or OXA-48-like carbapenemases.

References

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Acknowledgments

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Results

Figure 1a. Taxonomic grouping of Enterobacterales isolates collected in APAC, by phenotype

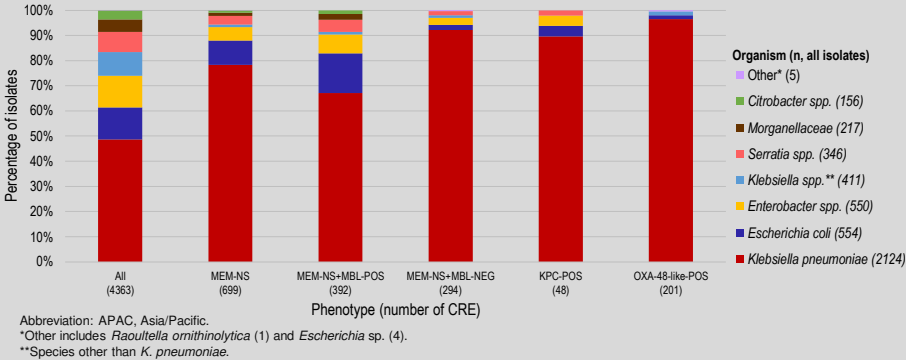


Figure 1b. Taxonomic grouping of Enterobacterales isolates collected in RoW, by phenotype

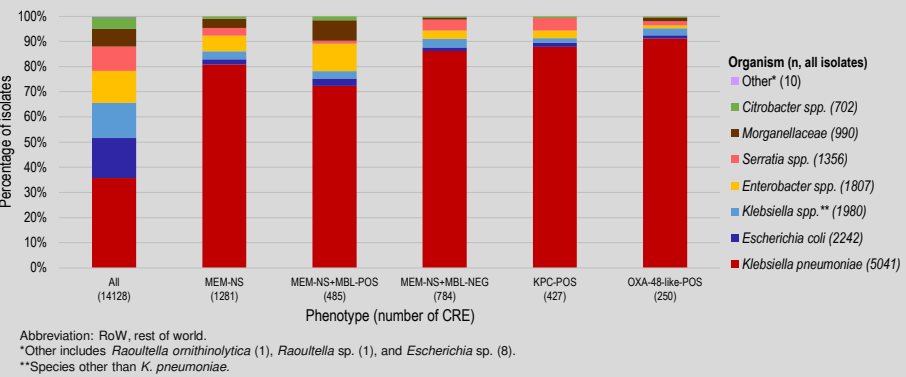


Figure 2. Percent CRE among isolates collected in APAC and RoW

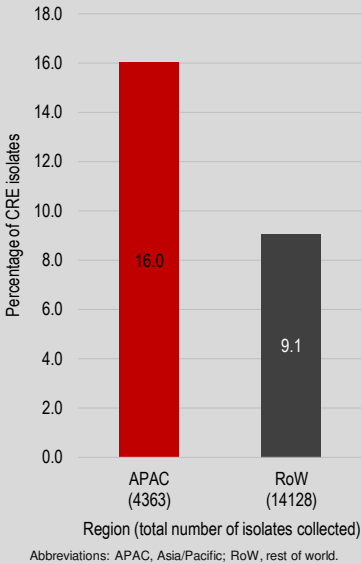


Figure 3. Carbapenemase carriage in Enterobacterales isolates from respiratory sources, by region

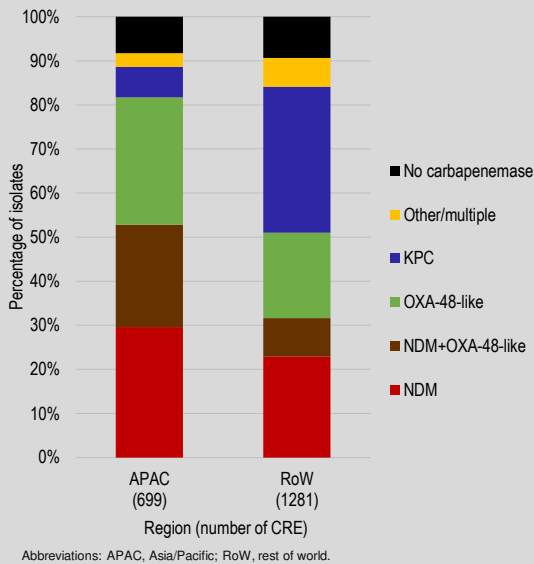


Table 1. *In vitro* activity of ceftazidime-avibactam and comparator agents against isolates collected in APAC versus RoW

		Agent, MIC ₉₀ (μg/mL), percent susceptible ^a																
		CAZ-AVI		CAZ		MEM		MEV		TGC		TZP		AMK		CST		
Region	Phenotype/Genotype	n	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%S	MIC ₉₀	%I ^b
APAC ^c	All	4363	16 ^e	90.0	>64	62.6	>16	84.0	>16	86.8	2	96.7	>64	69.1	>64	84.4	>8	83.6
	MEM-NS	699	>64	40.5	>64	1.3	>16	0.0	>16	17.7	2	93.1	>64	0.1	>64	29.5	>8	86.8
	MBL-	294	4	95.2	>64	3.1	>16	0.0	>16	31.6	2	94.2	>64	0.0	>64	33.3	8	88.1
	KPC+	48	4	97.9	>64	2.1	>16	0.0	4	95.8	4	89.6	>64	0.0	>64	62.5	>8	85.4
	OXA-48-like+	201	2	97.5	>64	2.5	>16	0.0	>16	8.0	2	96.5	>64	0.0	>64	24.4	2	90.0
RoW ^d	All	14128	1	96.3	>64	71.5	0.5	90.9	0.12	95.0	2	97.4	>64	74.2	8	89.5	>8	79.9
	MEM-NS	1281	>64	60.6	>64	4.5	>16	0.0	>16	45.2	2	94.4	>64	0.5	>64	35.9	>8	70.6
	MBL-	784	4	97.2	>64	7.1	>16	0.0	>16	66.8	2	94.3	>64	0.9	>64	45.5	>8	73.6
	KPC-POS	427	4	97.7	>64	1.6	>16	0.0	4	90.6	2	96.0	>64	0.2	>64	45.4	>8	71.9
	OXA-48-like+	250	2	98.4	>64	14.4	>16	0.0	>16	19.6	2	94.4	>64	0.0	>64	41.2	>8	71.2

Abbreviations: CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; MEM, meropenem; MEV, meropenem-vaborbactam; TGC, tigecycline; TZP, piperacillin-tazobactam; AMK, amikacin; CST, colistin; APAC, Asia/Pacific; RoW, rest of world; NS, non-susceptible; MBL-, metallo- β -lactamase negative; +, positive by PCR or WGS; S, susceptible; I, intermediate.

^a Susceptible using CLSI 2026 breakpoints. FDA breakpoints were used for tigecycline.

^b There is no susceptible breakpoint for colistin, the percent intermediate is shown.

^c APAC includes: Australia, Hong Kong, India (excluding 2024 isolates not available for molecular characterization), Japan, Malaysia, New Zealand, Philippines, South Korea, Taiwan, and Thailand.

^d Rest of world excludes the United States and Canada.

^e The MIC₉₀ of 16 μg/mL (resistant) appears discordant with the percentage susceptible due to rounding: 89.98% were susceptible.