RES-346

In Vitro Activity of Ceftazidime-avibactam and Comparator Agents Against Enterobacterales from Bloodstream Infections in Asia/Pacific: ATLAS Global Surveillance Program, 2019-2023

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Introduction

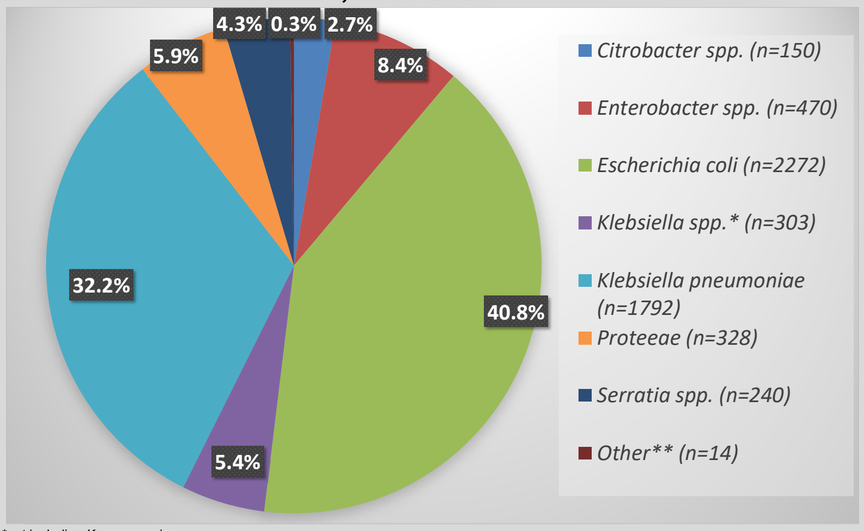
The β-lactamase inhibitor avibactam exhibits potent inhibitory activity against Class A, Class C, and some Class D serine β-lactamases and is approved for use with ceftazidime for several indications. This study evaluated the *in vitro* activity of ceftazidime-avibactam and comparators against Enterobacterales isolated from the blood of infected patients in the Asia/Pacific region collected as part of the Antimicrobial Testing Leadership and Surveillance (ATLAS) program [1] from 2019 to 2023.

Methods

- For ATLAS, a total of 5569 non-duplicate clinically significant Enterobacterales isolates from bloodstream infections were collected in 11 countries in the Asia/Pacific region (Australia, China, Hong Kong, India, Japan, Malaysia, New Zealand, Philippines, South Korea, Taiwan, Thailand) from 2019-2023 (Figure 1).
- Susceptibility testing was performed by broth microdilution following CLSI reference methodology [2] and interpreted with CLSI 2025 breakpoints [3].
- Most meropenem-nonsusceptible (MEM-NS) isolates, as well as most *Escherichia coli*, *Klebsiella pneumoniae*, *K. oxytoca*, *K. variicola* or *Proteus mirabilis* isolates testing with ceftazidime and/or aztreonam MIC values ≥2 µg/mL were screened for the presence of β-lactamase genes by PCR and Sanger sequencing, as previously described [4]. Qualifying isolates from China were not characterized molecularly for this study.

Results

Figure 1. Enterobacterales collected from bloodstream infections in Asia/Pacific, 2019-2023



*not including *K. pneumoniae*
**includes: *Escherichia* sp. (n=8), *Lelliottia amnigena* (n=1), *Raoultella ornithinolytica* (n=2), *Salmonella* sp. (n=3))

Table 1. *In vitro* activity of ceftazidime-avibactam and comparators against Enterobacterales from bloodstream infections in the Asia/Pacific region

Organism/Phenotype/Genotype (n)	Agent, [MIC_{90} (µg/ml), % Susceptible]											
	CZA		CAZ		MEM		TZP		C/T[a]		LVX	
	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S
All Enterobacterales (5569)	2	92.3	>64	65.1	16	88.7	>64	76.9	>16	82.2	>8	57.9
CAZ-NS (1941)	>64	78.0	>64	0	>16	67.7	>64	41.2	>16	49.0	>8	22.2
TZP-NS (1287)	>64	67.3	>64	11.3	>16	51.4	>64	0	>16	24.3	>8	18.9
C/T-NS (800)	>64	55.6	>64	2.1	>16	36.9	>64	3.8	>16	0	>8	14.0
LVX-NS (2343)	>64	83.4	>64	35.6	>16	74.6	>64	55.4	>16	63.2	>8	0
MEM-NS (631)	>64	34.5	>64	0.8	>16	0	>64	0.8	>16	0.8	>8	5.9
MEM-NS, MBL-Neg[b] (132)	4	92.4	>64	2.3	>16	0	>64	0.8	>16	0.9	>8	3.0

Abbreviations: CZA, ceftazidime-avibactam; CAZ, ceftazidime; MEM, meropenem; TZP, piperacillin-tazobactam; C/T, ceftolozane-tazobactam; LVX, levofloxacin; NS, non-susceptible; MBL, metallo-β-lactamase.
[a] C/T not tested in 2019 (for 2020-2023, n=4499).
[b] MEM-NS isolates collected in China were not molecularly characterized and thus not included here.

Figure 2. Susceptibility of Enterobacterales collected from bloodstream infections in Asia/Pacific to ceftazidime-avibactam and comparators (2019-2023), by country

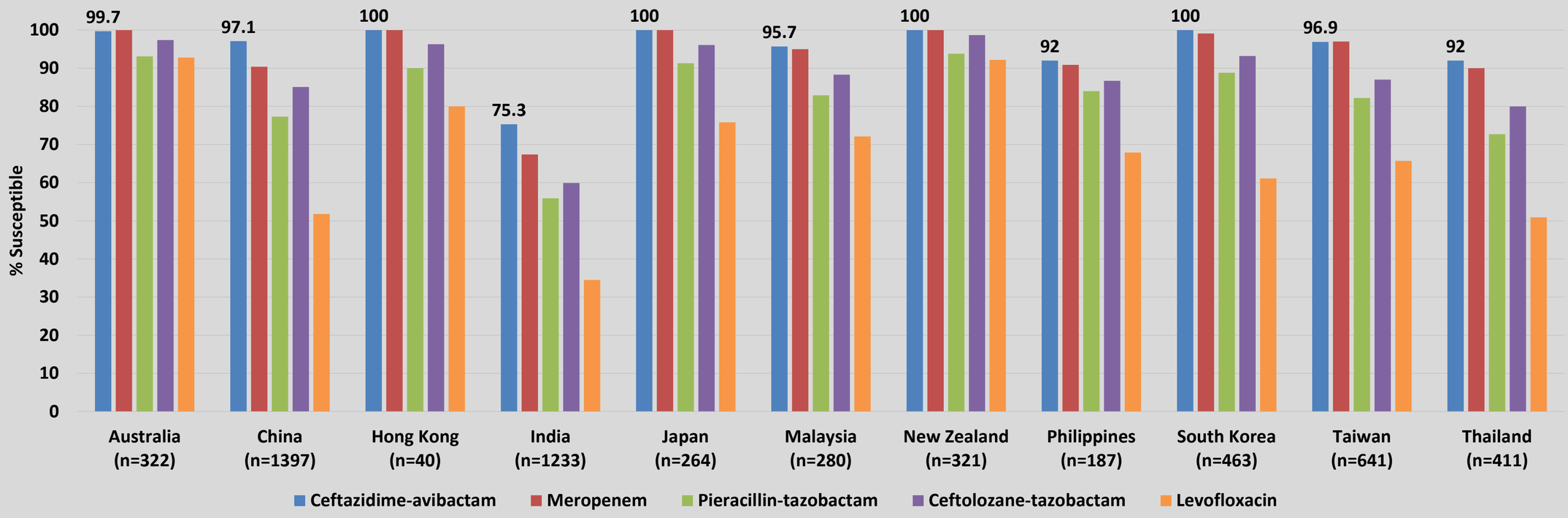
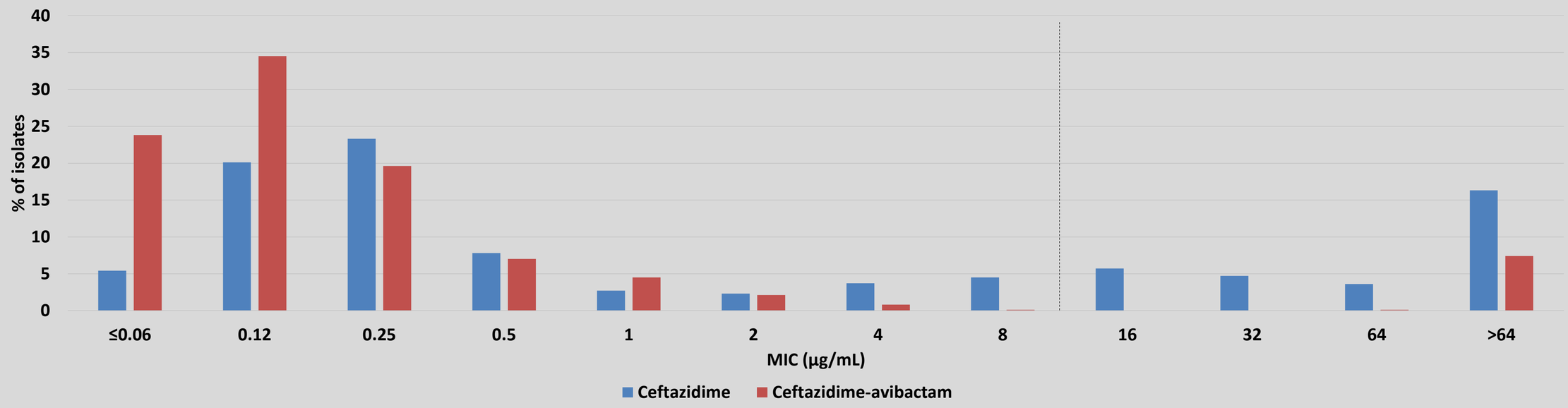


Figure 3. Ceftazidime and ceftazidime-avibactam MIC frequency distribution against 5569 Enterobacterales collected from patients with bloodstream infections in the Asia/Pacific region, 2019-2023



Dashed line indicates the CLSI susceptibility breakpoints for ceftazidime-avibactam

Results Summary

- Overall, 92.3% of isolates were susceptible to ceftazidime-avibactam (MIC_{90} = 2 µg/ml), an increase of >25 percentage points over ceftazidime alone (Table 1).
- Ceftazidime-avibactam was active against 78.0%, 67.3%, 55.6% and 83.4% of the ceftazidime-NS, piperacillin/tazobactam-NS, ceftolozane/tazobactam-NS and levofloxacin-NS isolates, respectively, in each case a higher percentage than comparators (Table 1).
- Versus meropenem-NS isolates, ceftazidime-avibactam was able to inhibit the growth of 34.5%; however, considering only those meropenem-NS isolates that were shown to be metallo-β-lactamase (MBL)-negative, the susceptibility rate increased to 92.4% (MIC_{90} = 4 µg/ml; Table 1).
- Analyses by individual country revealed that ceftazidime-avibactam inhibited >95% of Enterobacterales isolates from all countries except Philippines (92.0%), Thailand (92.0%) and India (75.3%), where it never-the-less was the most active antimicrobial agent among all comparators (Figure 2).
- MIC frequency graphs illustrate that adding avibactam to ceftazidime results in a substantial shift in the distribution toward the susceptible range (Figure 3).

Conclusions

Based on these *in vitro* data, ceftazidime-avibactam appears to provide a valuable therapeutic option for treating bloodstream infections caused by Enterobacterales, except those carrying MBLs.

References

1.Pfizer. *Antimicrobial Testing Leadership and Surveillance*. Available at: https://atlas-surveillance.com. Accessed September 2025.
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4.Lob SH, Kazmierczak KM, Badal RE, et al. 2015. *Trends in susceptibility of Escherichia coli from intra-abdominal infections to ertapenem and comparators in the United States according to data from the SMART program, 2009 to 2013*. Antimicrob Agents Chemother 59:3606-3610.

Disclosures

This study was sponsored by Pfizer. GS an KP are employees of Pfizer. MW and DS are employees of IHMA, which received fees from Pfizer for the conduct of the study and poster preparation.

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