RES-344

In Vitro Activity of Ceftazidime-avibactam Compared to Ceftolozane-tazobactam Against *Pseudomonas aeruginosa*, ATLAS Global Surveillance Program, 2020-2023

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Introduction

Avibactam is a β-lactamase inhibitor with potent inhibitory activity against Class A, Class C, and some Class D serine β-lactamases. The combination of ceftazidime with avibactam has been approved for several indications caused by gram-negative bacteria. This study examined the *in vitro* activity of ceftazidime-avibactam and comparators against *Pseudomonas aeruginosa* collected worldwide through the Antimicrobial Testing Leadership and Surveillance (ATLAS) global surveillance program [1] in 2020-2023 compared to the activity of ceftolozane-tazobactam.

Methods

28,138 non-duplicate *P. aeruginosa* isolates were collected from 209 sites/55 countries worldwide (excluding North America and China) as part of the ATLAS surveillance program from 2020 to 2023. Isolates were collected from (n/% of total): Europe (14,244/50.6%), Asia/S. Pacific (6,446/22.9%), Latin America (4,592/16.3%), and Africa/Middle East (2,856/10.2%). Susceptibility testing was done using broth microdilution following CLSI guidelines [2] and interpreted using CLSI 2025 breakpoints [3]. PCR and sequencing were used to identify metallo-β-lactamase (MBL) genes among all isolates testing with meropenem MIC >1 µg/mL [4].

Results

Table 1. *In vitro* activity of ceftazidime-avibactam, ceftolozane-tazobactam, and comparators against *Pseudomonas aeruginosa* and select phenotypes/genotypes

Phenotype/ Genotype (n)	Drug													
	CAZ-AVI		CAZ		C/T		MEM		TZP		LVX		CST	
	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%I[a]
All PA (28,138)	16	89.7	64	77.8	8	88.6	16	75.5	>64	74.2	>8	69.8	1	99.7
MEM NS (6,902)	>64	61.6	>64	38.8	>16	58.7	>16	0	>64	30.3	>8	26.6	1	99.5
MBL-neg (1,473)	32	79.2	>64	50	>16	77.1	>16	0.1	>64	39.8	>8	34.8	1	99.7
All, no MBL (27,710)	8	91.0	64	79	8	90.0	16	76.6	>64	75.3	>8	70.8	1	99.8
All, CT NS (3,208)	>64	21.9	>64	4.7	>16	0	>16	11.1	>64	6.4	>8	12.1	1	99.2
All, CAZ-AVI R (2,910)	>64	0	>64	0.4	>16	13.8	>16	9.0	>64	4.5	>8	10.8	1	99.3

MIC_{90} in µg/mL; CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; C/T, ceftolozane/tazobactam; MEM, meropenem; TZP, piperacillin-tazobactam; LVX, levofloxacin; CST, colistin; PA, *Pseudomonas aeruginosa*: S = susceptible; NS = non-susceptible; MBL = metallo-β-lactamase; NS, nonsusceptible; R = resistant
[a]As there is not a CLSI susceptible category for colistin, percent Intermediate is shown.

Figure 1. Distribution of ceftazidime-avibactam and ceftolozane-tazobactam MIC values against *Pseudomonas aeruginosa* (n=28,138), 2020-2023

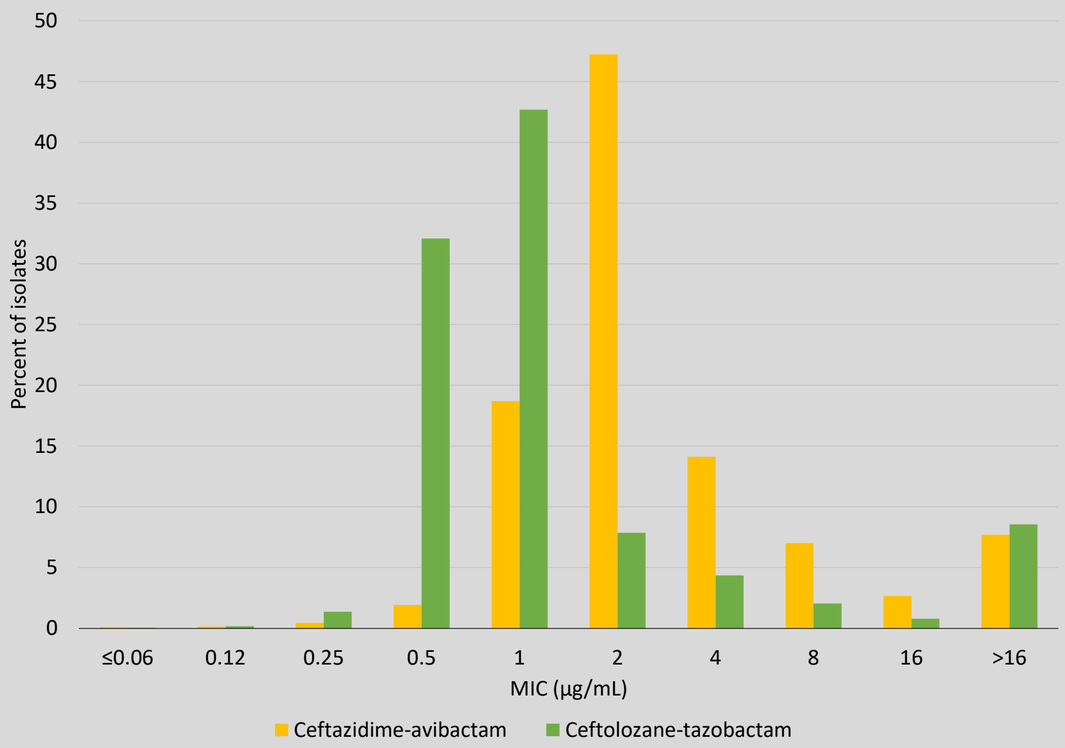


Figure 2. Distribution of ceftazidime-avibactam and ceftolozane-tazobactam MIC values against meropenem-nonsusceptible *Pseudomonas aeruginosa* (n=6,902), 2020-2023

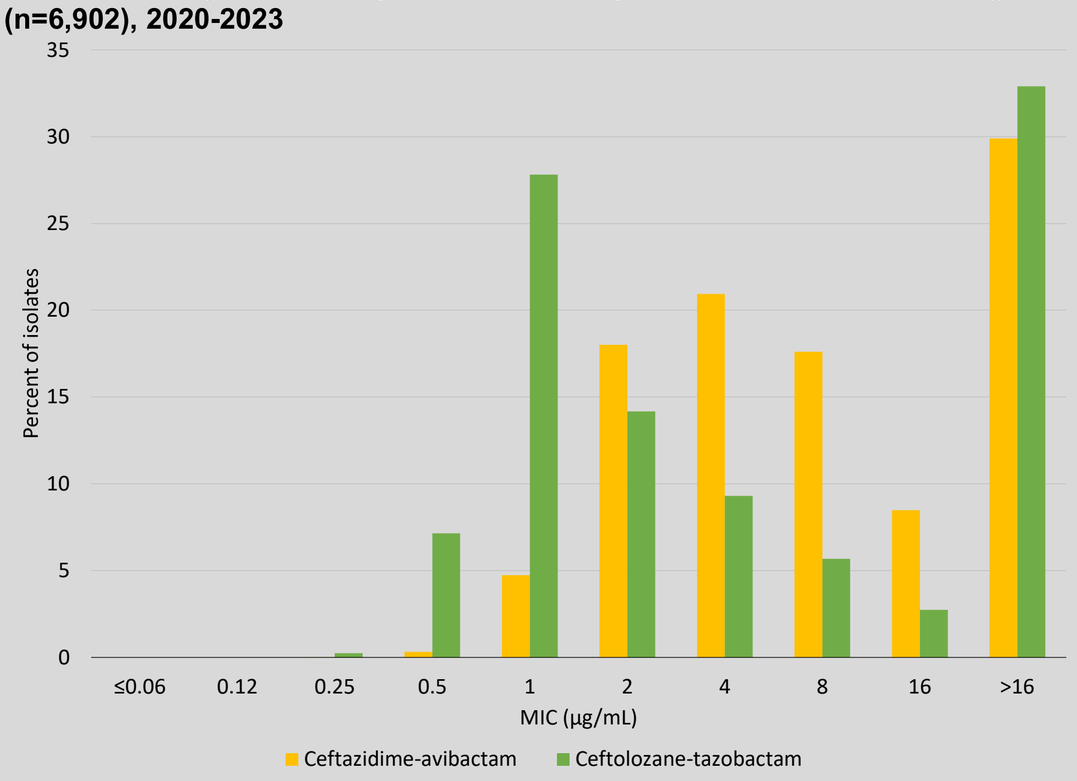


Figure 3. Distribution of ceftazidime-avibactam and ceftolozane-tazobactam MIC values against MBL-negative *Pseudomonas aeruginosa* (n=1,473), 2020-2023

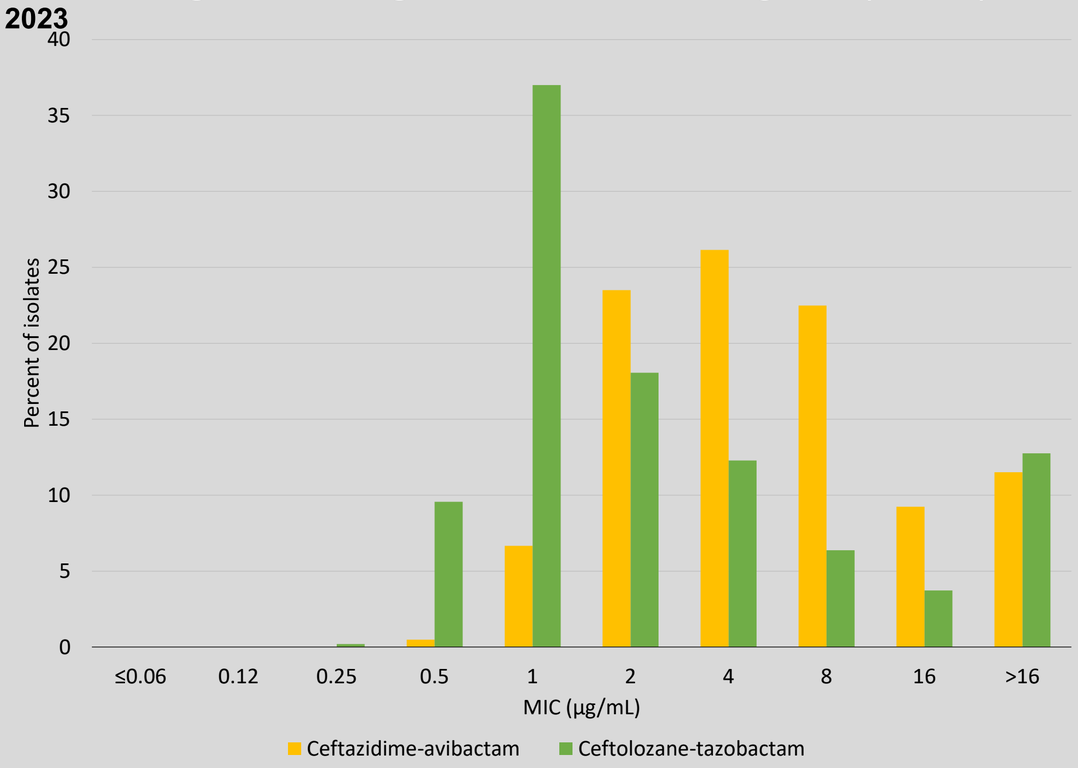
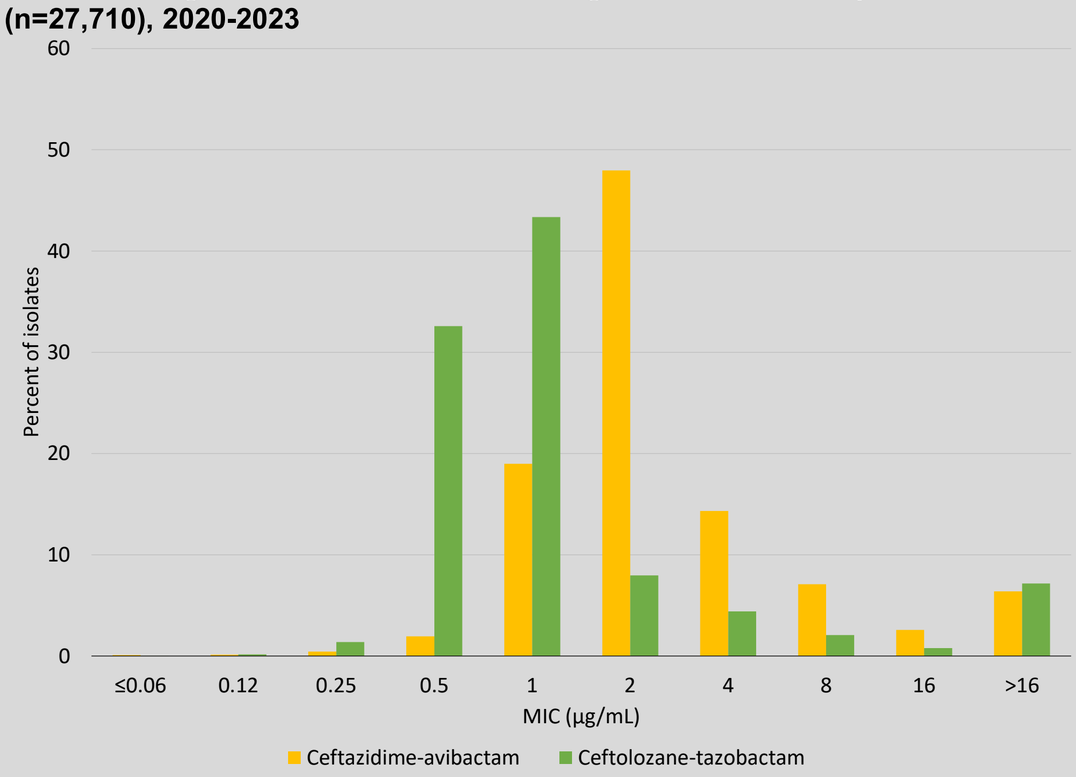


Figure 3. Distribution of ceftazidime-avibactam and ceftolozane-tazobactam MIC values against all *Pseudomonas aeruginosa* minus MBL-positive isolates (n=27,710), 2020-2023



Results Summary

- Among all *P. aeruginosa*, ceftazidime-avibactam showed good activity (89.7% susceptible, MIC_{90}=16 µg/mL). Activity of ceftolozane-tazobactam was similar (88.6% susceptible, MIC_{90}=8 µg/mL) (Table 1, Figure 1).
- Among all isolates, 24.5% were non-susceptible to meropenem, and of these, 61.6% were susceptible to ceftazidime-avibactam and 58.7% were susceptible to ceftolozane-tazobactam (Table 1, Figure 2).
- Of the 1,473 isolates that were molecularly screened (meropenem MIC >1 µg/mL) and were negative for MBL-producing genes, 79.2% were susceptible to ceftazidime-avibactam and 77.1% were susceptible to ceftolozane-tazobactam (Table 1, Figure 3).
- When MBL-producers were removed from all isolates tested, the percentage susceptible to ceftazidime-avibactam increased to 91.0% and the MIC_{90} decreased to 8 µg/mL. Ceftolozane-tazobactam showed similar activity against these isolates (90.0% susceptible, MIC_{90}=8 µg/mL) (Table 1, Figure 4).
- Among ceftolozane-tazobactam nonsusceptible isolates, 21.9% were susceptible to ceftazidime-avibactam, whereas among ceftazidime-avibactam resistant isolates, 13.8% were susceptible to ceftolozane-tazobactam (Table 1).

Conclusions

- Ceftazidime-avibactam demonstrated good *in vitro* activity against *P. aeruginosa* isolates.
- Ceftazidime-avibactam continues to be a useful therapeutic option for infections caused by *P. aeruginosa*, especially those not harboring MBLs.

References

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Disclosures

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

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