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In vitro Activity of Ceftazidime-Avibactam and Comparator Agents Against *Pseudomonas aeruginosa* Causing Intra-abdominal, Lower Respiratory, and Urinary Tract Infections Collected in Latin America as Part of the INFORM Global Surveillance Program, 2012-2016

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Introduction

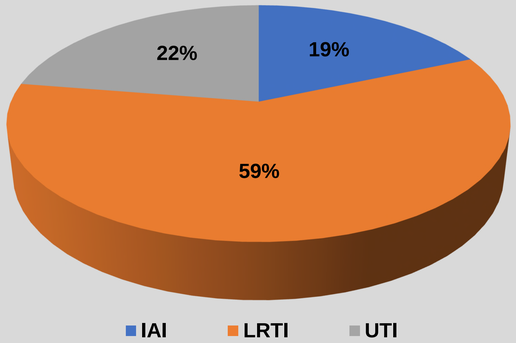
The non-β-lactam β-lactamase inhibitor avibactam is active against class A, class C and some class D β-lactamases, and in combination with ceftazidime has been approved by the FDA and EMA for treatment of intra-abdominal infections (IAI), lower respiratory tract infections (LRTI) and urinary tract infections (UTI). This study reports on the *in vitro* activity of ceftazidime-avibactam and comparators against *P. aeruginosa* isolates collected from IAIs, LRTIs and UTIs in Latin America as part of the International Network for Optimal Resistance Monitoring (INFORM) surveillance study from 2012-2016.

Methods

- 1,595 non-duplicate *P. aeruginosa* isolates linked to IAIs, LRTIs and UTIs were collected from 26 clinical sites in Argentina, Brazil, Chile, Colombia, Mexico and Venezuela.
- Susceptibility testing was done using broth microdilution according to CLSI guidelines and interpreted using CLSI 2018 breakpoints (1,2).
- Ceftazidime-avibactam was tested with a fixed concentration of 4 µg/ml avibactam.
- Meropenem non-susceptible organisms were screened for β-lactamase genes by PCR as described previously (3).

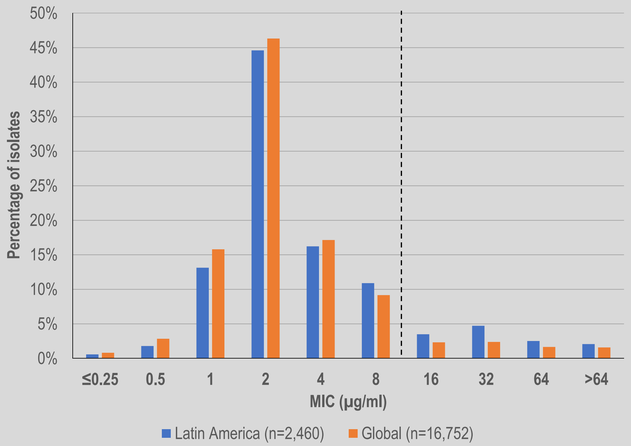
Results

Figure 1. *P. aeruginosa* infection sources of isolates examined in this study*



*IAI, intra-abdominal infections; LRTI, lower respiratory tract infections; UTI, urinary tract infections.

Figure 2. Ceftazidime-avibactam MIC distributions against *P. aeruginosa* collected both globally and solely in Latin America from 2012-2016*



†Dashed line represents CLSI susceptibility breakpoint of ≤8 µg/ml for ceftazidime-avibactam.

Table 1. *In vitro* activity of ceftazidime-avibactam and comparators against *P. aeruginosa* collected in Latin America from 2012-2016[a]

Region	Phenotype/Infection source (n)	Drug (MIC_{90} [µg/ml])/% Susceptible)							
		CAZ-AVI		CAZ		MEM		CST	
All Latin America	All sources (1,595)[b]	16	86.0	64	68.7	> 8	61.9	2	96.2
	IAI (295)	32	85.1	64	70.9	> 8	62.4	2	96.7
	LRTI (942)	16	86.8	128	69.3	> 8	60.7	2	96.3
	UTI (358)	32	84.6	64	65.1	> 8	64.8	2	95.8
	MBL-negative, All sources (1,488)[c]	8	91.9	64	73.5	> 8	66.1	2	96.1
	IAI (269)	8	93.3	64	77.7	> 8	68.0	2	96.4
	LRTI (889)	8	91.8	64	73.3	> 8	64.0	2	96.0
	UTI (330)	8	91.2	64	70.3	> 8	70.3	2	96.2
Argentina	All sources (268)	8	93.3	64	77.2	> 8	65.3	2	98.1
	IAI (32)	4	100	16	87.5	8	84.4	2	100
	LRTI (157)	8	91.7	64	78.3	> 8	59.2	2	98.4
	UTI (79)	8	93.7	64	70.9	> 8	69.6	2	97.0
	MBL-negative, All sources (263)	8	95.1	32	78.7	> 8	66.5	2	98.1
	IAI (32)	4	100	16	87.5	8	84.4	2	100
	LRTI (154)	8	93.5	32	79.9	> 8	60.4	2	98.4
	UTI (77)	8	96.1	64	72.7	> 8	71.4	2	96.9
Brazil	All sources (275)	8	92.4	64	71.3	> 8	66.2	2	95.0
	IAI (48)	8	95.8	32	77.1	> 8	66.7	2	93.3
	LRTI (170)	8	93.5	64	71.8	> 8	64.1	2	96.1
	UTI (57)	16	86.0	64	64.9	> 8	71.9	2	92.5
	MBL-negative, All sources (271)	8	93.7	64	72.3	> 8	67.2	2	94.9
	IAI (48)	8	95.8	32	77.1	> 8	66.7	2	93.3
	LRTI (168)	8	94.6	32	72.6	> 8	64.9	2	96.1
	UTI (55)	16	89.1	64	67.3	> 8	74.6	2	92.1
Chile	All sources (259)	32	75.7	128	50.2	> 8	53.3	2	97.1
	IAI (28)	32	78.6	> 128	60.7	> 8	60.7	2	100
	LRTI (138)	32	71.4	> 128	44.2	> 8	50.7	2	98.1
	UTI (93)	32	80.7	64	55.9	> 8	54.8	2	94.7
	MBL-negative, All sources (223)	16	87.9	128	58.3	> 8	60.5	2	97.7
	IAI (25)	16	88.0	> 128	68.0	> 8	68.0	2	100
	LRTI (115)	16	86.1	> 128	53.0	> 8	58.3	2	97.7
	UTI (83)	8	90.4	64	62.7	> 8	61.5	2	97.0
Colombia	All sources (159)	32	88.1	128	66.0	> 8	64.8	2	95.4
	IAI (39)	32	89.7	64	79.5	> 8	64.1	2	96.2
	LRTI (77)	8	92.2	128	64.9	> 8	66.2	2	92.0
	UTI (43)	32	79.1	128	55.8	> 8	62.8	2	100
	MBL-negative, All sources (148)	8	93.9	128	71.0	> 8	68.9	2	95.0
	IAI (36)	8	97.2	64	86.1	> 8	66.7	2	95.8
	LRTI (76)	8	92.1	128	65.8	> 8	67.1	2	92.0
	UTI (36)	8	94.4	128	66.7	> 8	75.0	2	100
Mexico	All sources (429)	64	85.3	> 128	71.1	> 8	59.4	2	95.3
	IAI (80)	64	83.8	> 128	65.0	> 8	55.0	2	97.0
	LRTI (285)	32	86.7	> 128	72.3	> 8	59.7	2	94.9
	UTI (64)	64	81.3	> 128	73.4	> 8	64.1	2	94.7
	MBL-negative, All sources (417)	32	87.5	> 128	72.9	> 8	61.2	2	95.1
	IAI (78)	32	85.9	> 128	66.7	> 8	56.4	2	96.9
	LRTI (278)	16	88.9	> 128	74.1	> 8	61.2	2	94.7
	UTI (61)	64	83.6	> 128	75.4	> 8	67.2	2	94.4
Venezuela	All sources (205)	32	81.0	64	74.2	> 8	65.9	2	96.8
	IAI (68)	32	72.1	64	64.7	> 8	57.4	2	95.6
	LRTI (115)	32	85.2	64	79.1	> 8	68.7	2	96.9
	UTI (22)	16	86.4	32	77.3	> 8	77.3	2	100
	MBL-negative, All sources (166)	4	98.8	8	91.0	> 8	81.3	2	96.1
	IAI (50)	4	98.0	32	88.0	> 8	78.0	2	93.9
	LRTI (98)	8	99.0	8	91.8	> 8	80.6	2	96.4
	UTI (18)	4	100	8	94.4	1	94.4	2	100

[a] CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; MEM, meropenem; CST, colistin; MBL, metallo-β-lactamase. % susceptible defined using CLSI 2018 breakpoints.
[b] CST not tested in 2012 or 2013; Totals for IAI, n=215; LRTI, n=721; UTI, n=286.
[c] CST not tested in 2012 or 2013; Totals for IAI, n=196; LRTI, n=677; UTI, n=260.

Results

- Ceftazidime-avibactam demonstrated greatest *in vitro* activity against *P. aeruginosa* from Argentina and Brazil (93.3% and 92.4% susceptible, respectively) while isolates from the remaining countries ranged from 75.7-88.1% susceptible (Table 1).
- A greater % of isolates were susceptible to ceftazidime-avibactam than to meropenem in every country (75.7-93.3% vs. 53.3-66.2% susceptible, respectively). Colistin was a potent comparator with 95.0-98.1% of isolates from all countries susceptible (Table 1).
- The activity of ceftazidime-avibactam was consistent among isolates from different specimen sources; 84.6-86.8% of isolates from IAI, LRTI and UTI were susceptible (Table 1).
- 4.9% more isolates from Latin America were resistant to ceftazidime-avibactam than from the global collection (Figure 2). This is at least partly due to the relatively large number of bla_{VIM-2} encoding isolates from this region.
- When MBL positive isolates were removed from analysis, the percentage of susceptibility rose to 91.2-93.3% across the different specimen sources (Table 1).

Conclusions

- Ceftazidime-avibactam demonstrated *in vitro* potency against those *P. aeruginosa* isolates which did not carry metallo-β-lactamases collected from IAI, LRTI, and UTI in Latin America from 2012-2016.
- Ceftazidime-avibactam remains a viable alternative to meropenem and colistin for the treatment of *P. aeruginosa* infections which are growing ever more resistant to available therapeutics.

References

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Disclosures

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