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In Vitro Activity of Ceftazidime-Avibactam and Comparator Agents Against MDR Enterobacterales and *Pseudomonas aeruginosa* Collected in Latin America During the ATLAS Global Surveillance Program 2017-2018

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Introduction

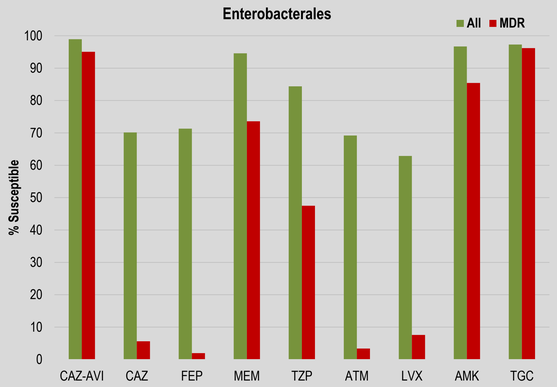
Ceftazidime-avibactam (CAZ-AVI) is a β-lactam/non-β-lactam β-lactamase inhibitor combination that can inhibit class A, C and some class D β-lactamases. Resistance caused by these β-lactamases often results in multidrug-resistance (MDR). This study evaluated the *in vitro* activity of CAZ-AVI and comparators against MDR Enterobacterales and *Pseudomonas aeruginosa* isolates collected from patients in Latin America.

Methods

Non-duplicate clinical isolates were collected in 2017-2018 in 10 countries in Latin America (Argentina, Brazil, Chile, Colombia, Costa Rica, Dominican Republic, Guatemala, Mexico, Panama, and Venezuela). Susceptibility testing was performed using CLSI broth microdilution and interpreted using CLSI 2020 and FDA (tigecycline) breakpoints [1-3]. MDR was defined as resistant (R) to ≥3 of 7 sentinel drugs: amikacin (AMK), aztreonam (ATM), cefepime (FEP), colistin (CST), levofloxacin (LVX), meropenem (MEM), and piperacillin-tazobactam (TZP).

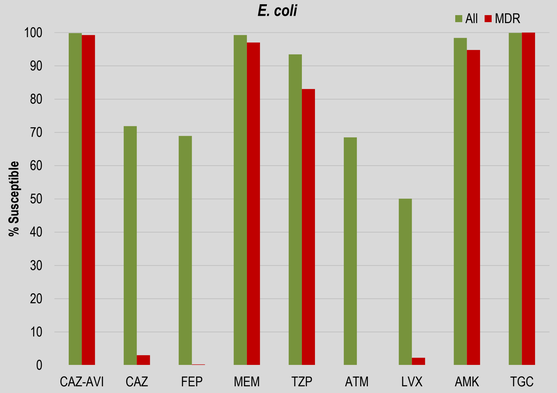
Results

Figure 1. Susceptibility to CAZ-AVI and comparators of all (n=5532) and MDR (n=1070, 19.3%) Enterobacterales isolates



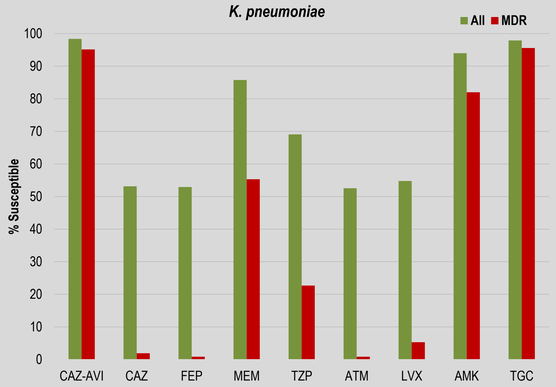
CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; FEP, cefepime; MEM, meropenem; TZP, piperacillin-tazobactam; ATM, aztreonam; LVX, levofloxacin; AMK, amikacin; TGC, tigecycline

Figure 2. Susceptibility to CAZ-AVI and comparators of all (n=1860) and MDR (n=401, 21.6%) *E. coli* isolates



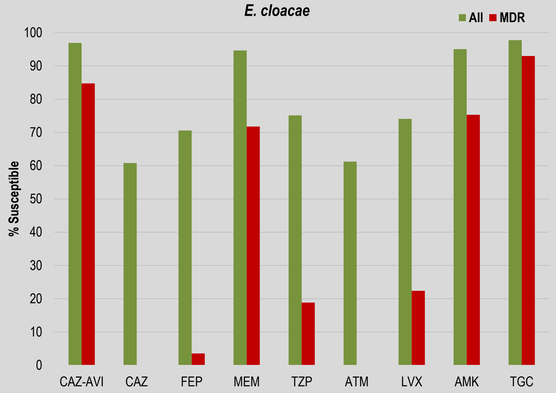
CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; FEP, cefepime; MEM, meropenem; TZP, piperacillin-tazobactam; ATM, aztreonam; LVX, levofloxacin; AMK, amikacin; TGC, tigecycline

Figure 3. Susceptibility to CAZ-AVI and comparators of all (n=1523) and MDR (n=472, 31.0%) *K. pneumoniae* isolates



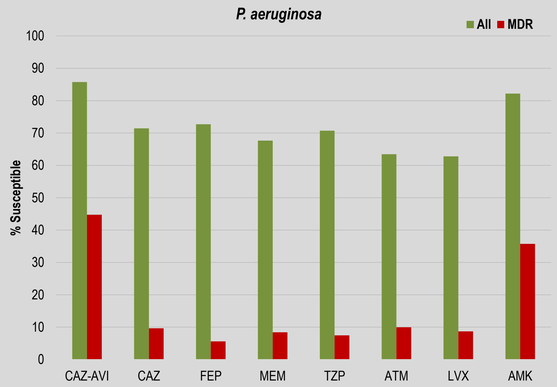
CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; FEP, cefepime; MEM, meropenem; TZP, piperacillin-tazobactam; ATM, aztreonam; LVX, levofloxacin; AMK, amikacin; TGC, tigecycline

Figure 4. Susceptibility to CAZ-AVI and comparators of all (n=482) and MDR (n=85, 17.6%) *E. cloacae* isolates



CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; FEP, cefepime; MEM, meropenem; TZP, piperacillin-tazobactam; ATM, aztreonam; LVX, levofloxacin; AMK, amikacin; TGC, tigecycline

Figure 5. Susceptibility to CAZ-AVI and comparators of all (n=1403) and MDR (n=322, 23.0%) *P. aeruginosa* isolates



CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; FEP, cefepime; MEM, meropenem; TZP, piperacillin-tazobactam; ATM, aztreonam; LVX, levofloxacin; AMK, amikacin.

Table 1. Combinations of nonsusceptible phenotypes most commonly observed among MDR isolates of Enterobacterales and *P. aeruginosa*

MDR phenotype[a]	n	% among all MDR isolates	% CAZ-AVI-susceptible
Enterobacterales			
1. ATM, FEP, LVX	538	50.3	100
2. ATM, FEP, LVX, MEM, TZP	112	10.5	88.4
3. ATM, FEP, LVX, TZP	111	10.4	100
4. ATM, CST, FEP, LVX, MEM, TZP	49	4.6	93.9
5. AMK, ATM, FEP, LVX, MEM, TZP	34	3.2	64.7
All MDR	1070	100	95.0
P. aeruginosa			
1. AMK, ATM, FEP, LVX, MEM, TZP	70	21.7	20.0
2. AMK, LVX, MEM	33	10.2	33.3
3. ATM, FEP, LVX, MEM, TZP	30	9.3	70.0
4. AMK, FEP, LVX, MEM	21	6.5	14.3
5. ATM, LVX, MEM	18	5.6	100
All MDR	322	100	44.7

[a]MDR phenotype, combination of ≥3 sentinel agents that tested as resistant against the indicated number of isolates. Sentinel agents not shown as part of an MDR phenotype tested with susceptible or intermediate MIC values.
Sentinel agents used to define MDR: AMK, amikacin; ATM, aztreonam; FEP, cefepime; CST, colistin; LVX, levofloxacin; MEM, meropenem; TZP, piperacillin-tazobactam.

Results

- MDR rates for the studied species ranged from 17.6% among *E. cloacae* to 31.0% among *K. pneumoniae* isolates (Figures 1-5).
- CAZ-AVI was active against 99% of Enterobacterales isolates and maintained activity against 85-99% of MDR isolates of the examined species. Only tigecycline showed comparable or higher activity (Figures 1-4).
- Among *P. aeruginosa*, CAZ-AVI was active against 86% of all isolates and 45% of MDR isolates; no other studied drug was more active (Figure 5).
- CAZ-AVI maintained activity against 65-100% of MDR Enterobacterales isolates and against 14-100% of MDR *P. aeruginosa* isolates displaying the five most commonly observed patterns of combined resistance to sentinel agents (Table 1).

Conclusions

These *in vitro* data suggest that CAZ-AVI can be an effective treatment option for infections caused by MDR Enterobacterales and *P. aeruginosa* collected in Latin America.

References

1. Clinical and Laboratory Standards Institute. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standards – Eleventh Edition*. CLSI document M07-Ed11. 2018. CLSI, Wayne, PA.
2. Clinical and Laboratory Standards Institute. *Performance Standards for Antimicrobial Susceptibility Testing – 30th ed*. CLSI Supplement M100. 2020. CLSI, Wayne, PA.
3. Pfizer Inc. 2016. *Tygacil (tigecycline) injection, powder, lyophilized, for solution, prescribing information*. Pfizer Inc., Collegeville, PA.

Disclosures

This study was sponsored by Pfizer. AZ's rights to ceftazidime-avibactam were acquired by Pfizer in December 2016. IHMA received financial support from Pfizer in connection with the study and the development of this poster. SL, KK and DS are employees of IHMA. GS, an employee of and shareholder in AZ at the time of the study, is currently an employee of Pfizer.

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