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In Vitro Activity of Ceftazidime-Avibactam and Comparator Agents Against MDR Enterobacterales and *Pseudomonas aeruginosa* Collected in Latin America, ATLAS Global Surveillance Program 2018-2020

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Introduction

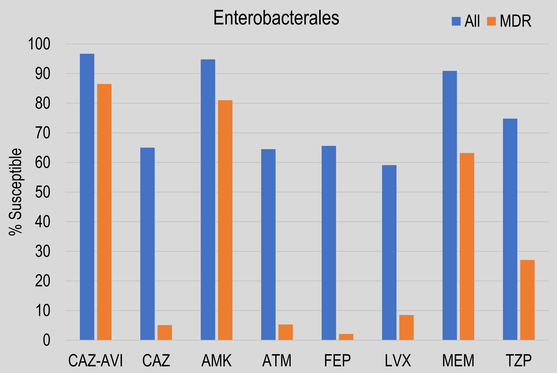
Multidrug-resistant (MDR) Gram-negative bacteria are an increasing worldwide problem. Ceftazidime-avibactam (CAZ-AVI) is a β-lactam/non-β-lactam β-lactamase inhibitor combination that can inhibit class A, C, and some class D β-lactamases, enzymes that contribute to MDR. This study examined the *in vitro* activity of CAZ-AVI and comparator against MDR Enterobacterales and *Pseudomonas aeruginosa* isolates collected from patients in Latin America as part of the ATLAS Global Surveillance Program in 2018-2020.

Methods

9193 non-duplicate Enterobacterales and 3225 *P. aeruginosa* isolates from were collected from 36 sites in 10 Latin American countries (Argentina, Brazil, Chile, Colombia, Costa Rica, Dominican Republic, Guatemala, Mexico, Panama, and Venezuela) as part of ATLAS 2018-2020. Antimicrobial susceptibility testing was by broth microdilution according to CLSI guidelines and interpreted using CLSI 2022 MIC breakpoints [1,2]. 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).

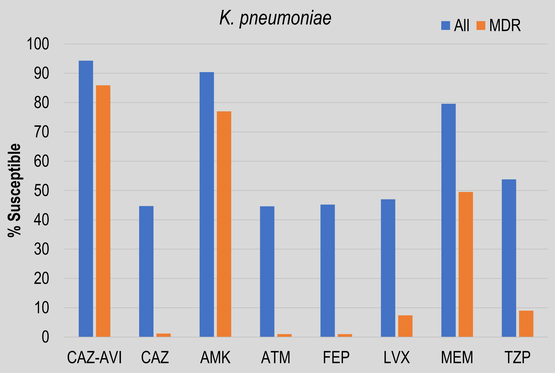
Results

Fig 1. Susceptibility to CAZ-AVI and comparators of all (n=9193) and MDR (n=2194, 23.7%) Enterobacterales isolates



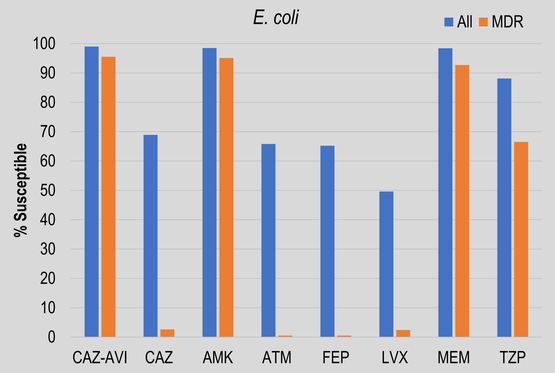
CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; AMK, amikacin; ATM, aztreonam; FEP, cefepime; LVX, levofloxacin; MEM, meropenem; TZP, piperacillin-tazobactam

Fig 2. Susceptibility to CAZ-AVI and comparators of all (n=2818) and MDR (n=1128, 40.0%) *K. pneumoniae* isolates



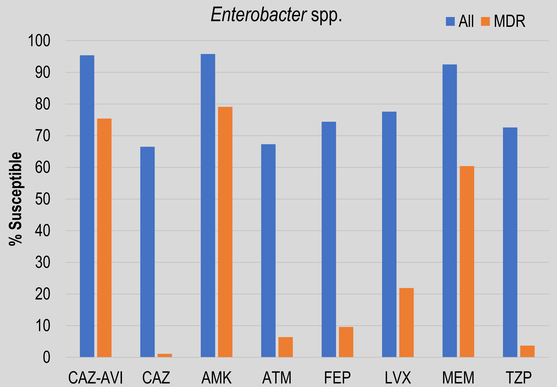
CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; AMK, amikacin; ATM, aztreonam; FEP, cefepime; LVX, levofloxacin; MEM, meropenem; TZP, piperacillin-tazobactam

Fig 3. Susceptibility to CAZ-AVI and comparators of all (n=2857) and MDR (n=617, 21.6%) *E. coli* isolates



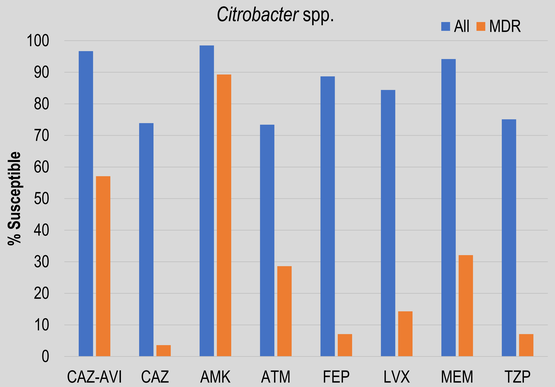
CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; AMK, amikacin; ATM, aztreonam; FEP, cefepime; LVX, levofloxacin; MEM, meropenem; TZP, piperacillin-tazobactam

Fig 4. Susceptibility to CAZ-AVI and comparators of all (n=1097) and MDR (n=187, 17.0%) *Enterobacter* spp. isolates



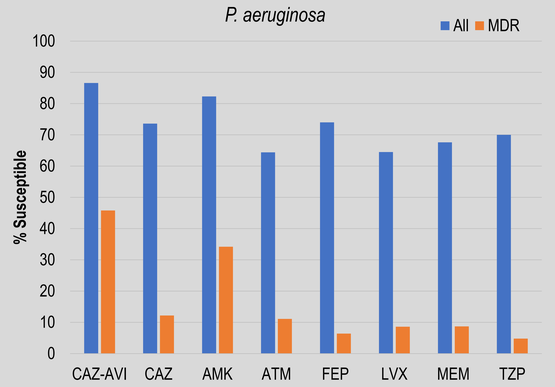
CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; AMK, amikacin; ATM, aztreonam; FEP, cefepime; LVX, levofloxacin; MEM, meropenem; TZP, piperacillin-tazobactam

Fig 5. Susceptibility to CAZ-AVI and comparators of all (n=398) and MDR (n=28, 7.0%) *Citrobacter* spp. isolates



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

Fig 6. Susceptibility to CAZ-AVI and comparators of all (n=3225) and MDR (n=732, 22.7%) *P. aeruginosa* isolates



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

Results

- The MDR rate for the overall collection of Enterobacterales was 23.7%, and for *K. pneumoniae*, *E. coli*, *Enterobacter* spp. and *Citrobacter* spp. the MDR rates were 40.0%, 21.6%, 17.0% and 7.0%, respectively. For *P. aeruginosa*, the MDR rate was 22.7%.
- CAZ-AVI was active against the full collection of Enterobacterales isolates with 96.7% of the population susceptible and an MIC_{90} value of 1 µg/mL, and maintained considerable activity against the MDR subset, inhibiting 86.5% of the isolates, a value higher than comparator agents (Fig. 1).
- Among the individual Enterobacterales species and genera examined, CAZ-AVI inhibited 95.5 – 57.1% of the MDR isolates (Fig. 2-5). For *K. pneumoniae* and *E. coli*, CAZ-AVI was the most active antimicrobial among comparator agents. Against MDR *Enterobacter* spp. and *Citrobacter* spp., only amikacin was more active.
- For the full collection of *P. aeruginosa*, 86.6% of the isolates were susceptible to CAZ-AVI, the highest susceptibility percentage among the comparator agents. Versus the MDR subset of *P. aeruginosa*, CAZ-AVI displayed a 45.8% susceptibility rate, approximately 10 percentage points higher than the nearest comparator, amikacin (Fig. 6).

Conclusions

The *in vitro* data suggest that CAZ-AVI can be an effective therapeutic option for infections caused by MDR Enterobacterales in Latin America. MDR among *P. aeruginosa* remains challenging, although the growth of a significant percentage is inhibited by CAZ-AVI *in vitro*.

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 – 31st ed*. CLSI Supplement M100. 2021. CLSI, Wayne, 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. MW 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.