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In Vitro Activity of Ceftazidime-Avibactam and Comparator Agents Against Enterobacterales from ICU and Non-ICU Wards Collected in Latin America and Globally as part of the ATLAS Surveillance Program 2017-2018

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Introduction

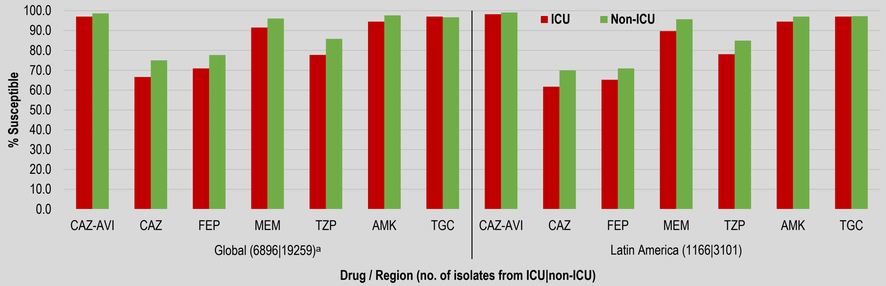
Ceftazidime-avibactam (CAZ-AVI) is a β-lactam/non-β-lactam β-lactamase inhibitor combination that inhibits class A, C and some class D β-lactamases but not class B metallo-β-lactamases (MBLs). Antimicrobial resistance due to production of these β-lactamases and other mechanisms is increasing and is especially high among isolates found in ICUs. This study evaluated the *in vitro* activity of CAZ-AVI and comparators against Entero-bacterales isolates from patients in ICU and non-ICU wards.

Methods

Non-duplicate clinical isolates were collected in 2017-2018 from patients in 51 countries in Asia/Pacific (excluding mainland China), Europe, Latin America (Argentina, Brazil, Chile, Colombia, Costa Rica, Dominican Republic, Guatemala, Mexico, Panama, and Venezuela), and Middle East/Africa. Susceptibility testing was performed using CLSI broth microdilution and interpreted using 2020 CLSI and FDA (tigecycline) breakpoints [1-3]. PCR and sequencing were used to determine the β-lactamase genes present in all isolates with meropenem (MEM) MIC >1 µg/ml, and *Escherichia coli*, *Klebsiella* spp. and *Proteus mirabilis* with aztreonam or ceftazidime MIC >1 µg/ml [4].

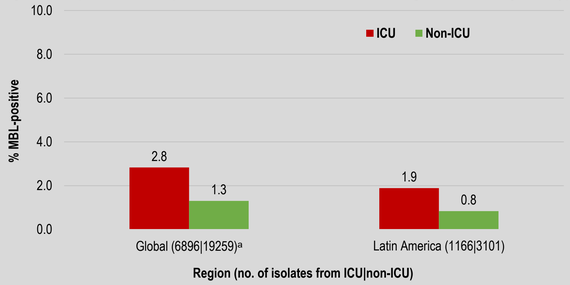
Results

Figure 1. Antimicrobial susceptibility of all Enterobacterales isolates



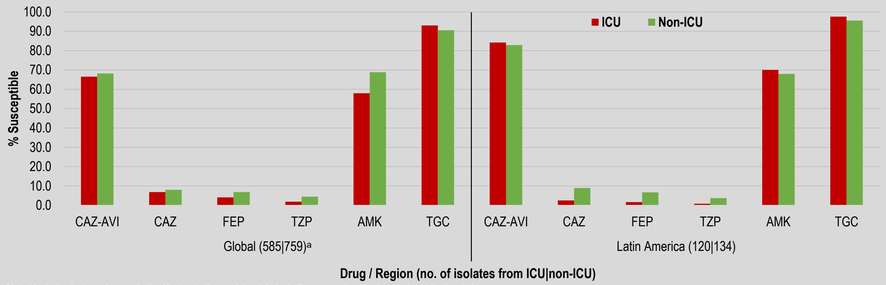
[a]Global includes isolates from Asia/Pacific (excluding mainland China), Europe, Latin America, and Middle East/Africa
CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; FEP, cefepime; MEM, meropenem; TZP, piperacillin-tazobactam; AMK, amikacin; TGC, tigecycline

Figure 2. Proportion of MBL-positive Enterobacterales isolates among all collected, by ward type



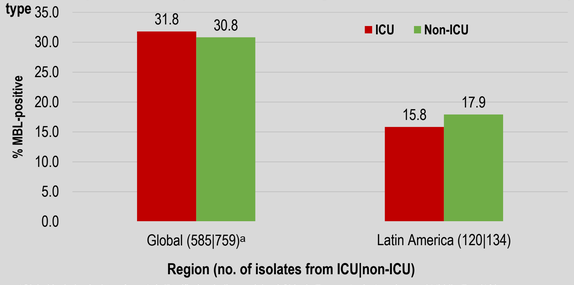
[a]Global includes isolates from Asia/Pacific (excluding mainland China), Europe, Latin America, and Middle East/Africa

Figure 3. Antimicrobial susceptibility of meropenem-nonsusceptible (MEM-NS) Enterobacterales isolates



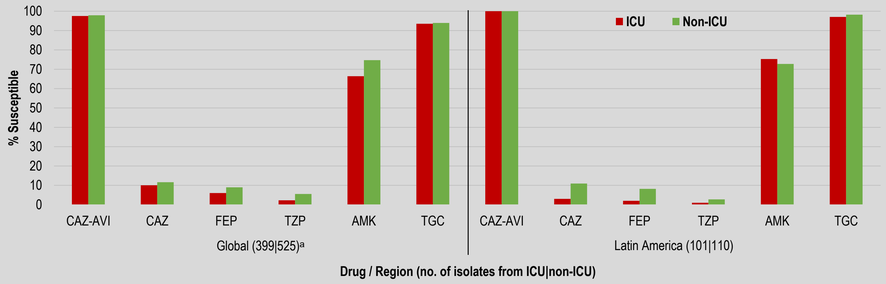
[a]Global includes isolates from Asia/Pacific (excluding mainland China), Europe, Latin America, and Middle East/Africa
CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; FEP, cefepime; TZP, piperacillin-tazobactam; AMK, amikacin; TGC, tigecycline

Figure 4. Proportion of MBL-positive isolates among MEM-NS Enterobacterales collected, by ward type



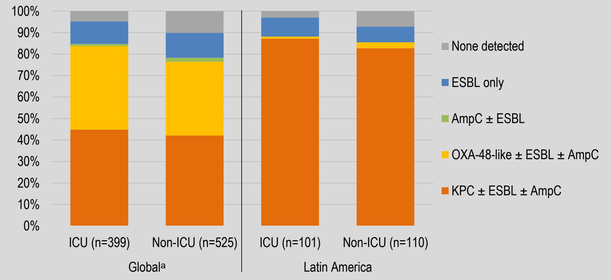
[a]Global includes isolates from Asia/Pacific (excluding mainland China), Europe, Latin America, and Middle East/Africa

Figure 5. Antimicrobial susceptibility of MEM-NS MBL-negative Enterobacterales isolates



[a]Global includes isolates from Asia/Pacific (excluding mainland China), Europe, Latin America, and Middle East/Africa
CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; FEP, cefepime; TZP, piperacillin-tazobactam; AMK, amikacin; TGC, tigecycline

Figure 6. Acquired β-lactamases detected among MEM-NS MBL-negative Enterobacterales isolates from ICU and non-ICU wards



[a]Global includes isolates from Asia/Pacific (excluding mainland China), Europe, Latin America, and Middle East/Africa

Results

- Susceptibility rates among global Enterobacterales were generally lower for isolates from patients in ICU than non-ICU wards, but this difference was small for CAZ-AVI (97.0% and 98.6% susceptible, respectively) and tigecycline. For isolates from Latin America (LA), antimicrobial activity was generally similar to the global average, with slightly higher susceptibility to CAZ-AVI of 98.2% (ICU) and 99.1% (non-ICU) (Figure 1).
- The proportion of MBL-positive isolates was higher among ICU patients than non-ICU patients both globally and in LA. MBL rates were about 1 percentage point lower in LA than globally (Figure 2).
- Among MEM-nonsusceptible (NS) isolates, ICU/non-ICU differences in susceptibility were generally small with CAZ-AVI active against 67-68% of isolates. As Enterobacterales are no longer considered susceptible to colistin per the 2020 CLSI guidelines [2], only tigecycline exceeded the activity of CAZ-AVI (Figure 3).
- The activity of CAZ-AVI was about 15 percentage points higher against MEM-NS isolates in LA than globally (Figure 3). Correspondingly, the proportion of MBL-positive isolates was about 15 percentage points lower among isolates collected in LA than the global average (Figure 4).
- CAZ-AVI inhibited >97% of MEM-NS MBL-negative isolates collected globally from patients in both ward types and 100% of isolates from LA. None of the tested comparators approached the activity of CAZ-AVI except tigecycline (Figure 5).
- Among MEM-NS MBL-negative isolates from LA, >80% from both ward types carried KPC enzymes, while globally KPC and OXA-48-like carbapenemases made up 42-45% and 34-39% of these isolates, respectively (Figure 6).

Conclusions

CAZ-AVI showed potent antimicrobial activity against Enterobacterales isolates collected from patients in both ICU and non-ICU wards, with ≥97% and >98% of all isolates collected globally and in LA, respectively, testing as susceptible. CAZ-AVI provides a valuable treatment option for infections caused by Enterobacterales that do not carry MBLs, including those among patients in ICU wards, where antimicrobial resistance is typically higher.

References

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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. S. Lob, K. Kazmierczak and D. Sahm are employees of IHMA. G. Stone, an employee of and shareholder in AZ at the time of the study, is currently an employee of Pfizer.

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