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P2779 Assessment of ceftazidime-avibactam CLSI 30/20 ug and EUCAST 10/4 ug disk content versus reference agar dilution/broth microdilution MIC results against Enterobacteriales and *Pseudomonas aeruginosa*

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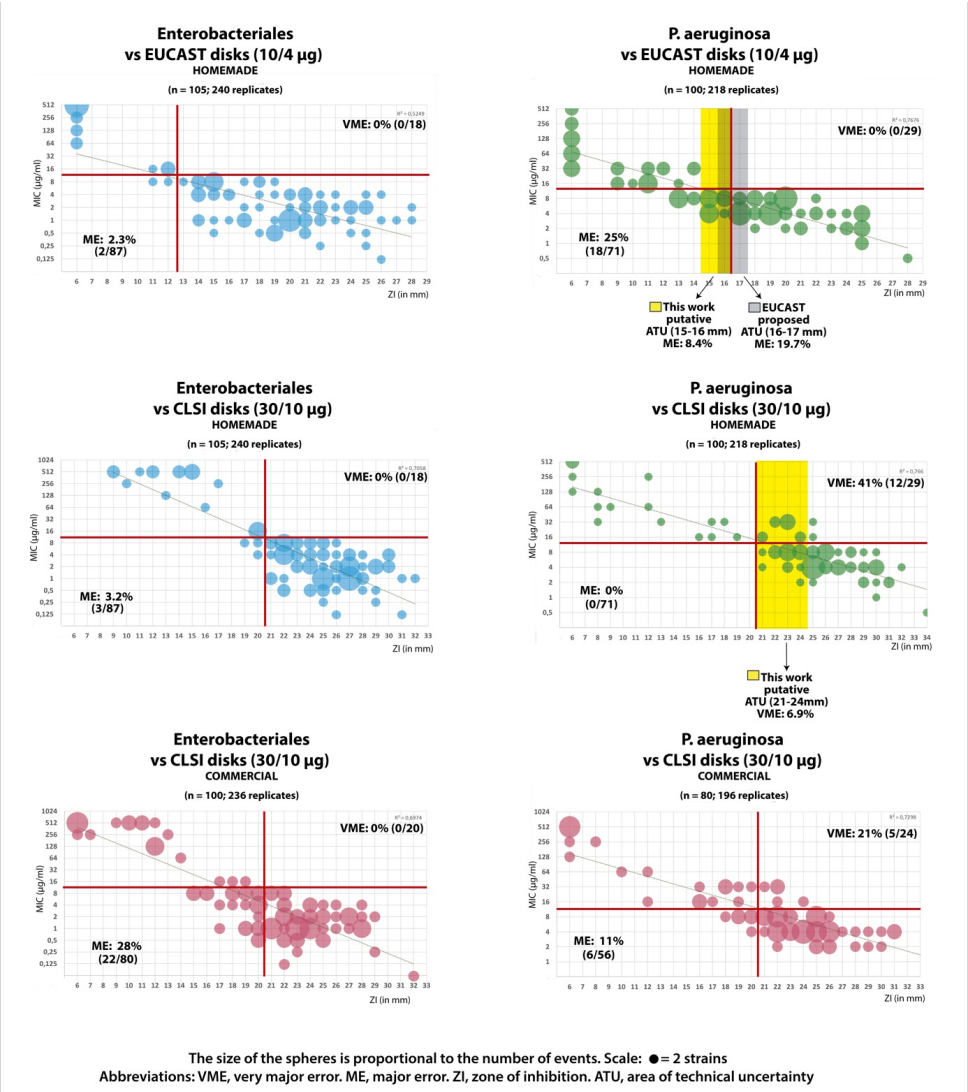
Background: Ceftazidime-avibactam (CZA) is active against ETB and PAE, including isolates that produce classes A, C, and some D β-lactamases. CZA disk content used for in vitro susceptibility testing differs between CLSI (30/20 µg) and EUCAST (10/4 µg). The studies described here relate to the disk mass selection that allows the best classification of CZA susceptibility among candidate strains for CZA (carbapenemase-producing and/or carbapenem-resistant ETB and PAE).

Materials/methods: 205 clinical isolates (100 PAE, 58 *Klebsiella*, 19 *Enterobacter*, 7 *Escherichia coli* and 21 from other species) collected from Argentina Hospitals (2016-2018) were included, along with ATCC strains *K. pneumoniae* 700603, PAE 27853, *E. coli* 25922. The molecular characterization of β-lactamases was performed by PCR/sequencing. The disk diffusion, agar dilution and microdilution tests followed CLSI/EUCAST standardized methods and were performed in duplicates, while ATCC strains were tested six-times. CLSI/EUCAST recommended disks masses were in-house prepared using powder solutions (Molekula). In addition, we tested commercially available 30/20 µg disks (Liofilchem). Time-kill curves were performed to solve MIC categories for strains with replicas between 8-16 µg/ml. Results were interpreted with breakpoints provided by the respective standard. Disk performances were evaluated using FDA criteria.



The size of the spheres is proportional to the number of events. Scale: ● = 2 strains
Abbreviations: VME, very major error. ME, major error. ZI, zone of inhibition. ATU, area of technical uncertainty

Results: 446 correlates were obtained. All replicas zones were within ± 2mm (96.8% ± 1mm). All disks type gave in-range results with ATCC strains. Performances depicted in Figure.

Conclusions: Both disk masses, when produced in-house, showed acceptable results against ETB. However, with CLSI disks (but not with EUCAST) a high number of susceptible replicas were observed close to the cutoff, which could affect the disk performance if a slight mass deterioration occurs, as seems to happen with commercial disks. ATCC strains did not alert of the poor performance of commercial disks. Both, CLSI/EUCAST disks failed to correctly classified PAE isolates, with unacceptable levels of very major and major errors, respectively. Our data support the need for the inclusion of an area of technical uncertainty (ATU) for PAE, although the results interpreted with these ATUs will show some improvement, they will still have performance below standards. CZA susceptibility tests for PAE should be urgently reviewed to avoid miss-classifications to a last-resort drug.