Comparative evaluation of Meropenem/Vaborbactam MIC determination with the new ETEST® MEV* and CLSI broth microdilution method

For Research Use Only. The performance characteristics of this product have still not been established.

**BACKGROUND**

Carbapenem antibiotics are still a key weapon in the fight against β-lactam resistant Gram-negative infections. However, the increase of carbapenem-resistant Enterobacteriaceae (CRE) has become a global public health problem. This phenomenon has led to the development of new drug and inhibitor combinations, such as Meropenem/Vaborbactam. Vaborbactam (Melinta Therapeutics) is FDA approved for the treatment of adults with complicated urinary tract infections (cUTI) including pyelonephritis caused by the following susceptible microorganisms: Escherichia coli, Klebsiella pneumoniae and Enterobacter cloacae species complex.

The new ETEST® MEV (Meropenem/Vaborbactam - MIC range 0.004/8-64/8 µg/mL) has been developed and calibrated versus the broth microdilution reference method (BMD) as described by the Clinical and Laboratory Standards Institute (CLSI). This test is intended to determine the MIC of Meropenem/Vaborbactam toward the Enterobacteriaceae group.

**OBJECTIVE**

The aim of this study was to perform a comparative study of ETEST MEV with the CLSI Broth Microdilution method on a specific panel of 225 strains.

**METHODS**

- The panel includes 198 Enterobacteriaceae (among them 23 resistant strains to MEV,) 22 Pseudomonas aeruginosa, and 5 C. difficile strains.
- The details of QC strains and panel are presented in Tables 1 and 2.
- The strains were provided by bioMérieux internal collection; The Medicines Company diversity panel; and the CDC collection (Enterobacteriaceae Carbapenem Breakpoint panel – Gram Negative Carbapenemase Detection Panel – Enterobacteriaceae Carbapenemase Diversity Panel).
- The selected panel consisted of a majority of MDR strains. Among them: 135 strains with resistant genes to carbapenam such as KPC (92 strains), NDM, VIM, IMP (25 strains), OXA-48 (16 strains). Other resistance mechanisms or combinations with carbapenem resistance are represented: ESBL, strains with impermeability, AmpCs as well as wild type strains.

BMD was performed using the 2017 CLSI recommendations for Meropenem/Vaborbactam. ETEST MEV was evaluated using the standard ETEST MIC procedure for aerobic strains (incubation 0.5 McF from 18/24h cultures on Columbia agar±5% sheep blood, testing at 35°C during 16-20h). For each method, the MIC was read at complete inhibition of growth.

The FDA approved breakpoints for Enterobacteriaceae were applied: 0.54 µg/mL – 1.8 µg/mL – 8 µg/mL.

**RESULTS**

**Bacterial reading**

The MICs for QC strains are within the expected CLSI ranges with reproducible results. Ellipses are easy to read, clear, without trailing.

The essential MIC agreement ([± 1 dilution]) is 94.5% without overestimation or underestimation trend between ETEST MEV and BMD (see Table 3).

The global distribution shows that discrepancies are linked to high MIC values, without trend to over or underestimate (see Table 4).

**CONCLUSION**

In this study, the new ETEST MEV is found to be substantially equivalent to the CLSI reference method, MIC end points are easy to read. With a 15-dilution range and simplicity of use, ETEST MEV represents a valuable tool for MIC determination and is an alternative to the BMD reference method. ETEST MEV is currently under clinical studies in order to be IVD cleared (FDA and CE).