# Meropenem susceptibility testing – Comparison of broth microdilution and VITEK2 in a multicenter study - results from the NordicAST CPE 2016 study

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## *Objective*

Automated antimicrobial susceptibility testing (AST) methods are frequently used in clinical microbiology laboratories. The aim of this study was to compare the categorical agreement of meropenem (MEM) susceptibility obtained with broth microdilution (BMD) and VITEK2 in a multicenter study.

## *Methods*

As part of the NordicAST CPE 2016 multicenter study, laboratories using an automated AST device were invited to report MEM MIC and susceptibility category on a genetically characterized collection of carbapenemase positive (*n*=21) and negative (*n*=8) *Enterobacteriaceae* with reduced susceptibility to MEM (MIC 0.25 - ≥16 mg/L) (Table 1). 20/61 laboratories (Finland *n*=6, Norway *n*=9 and Sweden *n*=5) reported MICs and interpretations from VITEK2 (bioMérieux). The following AST cards were used in the respective countries; Finland AST-N230, Norway AST-N209 and Sweden AST-N218. The MEM MICs of the isolates were determined by BMD (Thermo Scientific Sensititre plates). Categorical agreement; very major (VME, R to S), major (ME, S to R) and minor (mE, R or S to I, or vice versa) errors was calculated according to ISO 20776-2 based on EUCAST clinical breakpoints v. 6.0. Each MEM MIC reported by the participating laboratories was interpreted as a single case (559 observations).

**Table 1. Strain collection**

| **Carbapenemase positive (*n*)** | **Carbapenemase (*n*)** |
|---|---|
| *Klebsiella* spp. (11) | KPC (1); VIM (2); NDM (1); NDM+OXA-181 (1); OXA-48-like (6)* |
| *E. coli* (5) | VIM (1); NDM (1); IMP (1); OXA-48-like (2) |
| *Enterobacter* spp. (3) | KPC (2); IMI (1) |
| *Citrobacter* spp. (1) | NDM (1) |
| *P. mirabilis* (1) | NDM (1) |
| **Carbapenemase negative (*n*)** | |
| *Klebsiella* spp. (2); *E. coli* (2); *Enterobacter* spp. (2); *P. mirabilis* (1); *P. rettgeri* (1) | |

*One *K. variicola* strain with $bla_{OXA-48-like}$ (MEM MIC 0.5 mg/L) was provided in triplicate.

## *Results*

The overall MEM categorical agreement between BMD and VITEK2 MIC was 58% (Table 2 and 3). No VME were observed. ME and mE were found in 25% and 17% of the cases, respectively. The number of ME and mE varied depending on the mechanism of reduced susceptibility to meropenem. For strains with class A and class B carbapenemases, ME were observed in 50% and 55% of the cases, respectively. For strains with class D OXA-48-like carbapenemases ME were only detected in 2.5% of cases and no ME were observed with the carbapenemase-negative strains. mE were observed in 25% (class A carbapenemase-producers), 7% (class B carbapenemase-producers), 35% (OXA-48-like-producers) and 20% (carbapenemase-negative) of cases. All mE were from S to I in the carbapenemase-positive strains, while for the carbapenemase-negative strains both S to I (62.5%) and I to S (37.5%) mE were observed.

**Table 2. MEM MIC agreement between BMD and Vitek2 (559 observations).**

| VITEK2 MIC mg/L | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | **>=16** | 21 | 1 | 78 | 40 | | 20 | **80** |
| | **8** | | | | 2 | 8 | **7** | |
| | **4** | 4 | 15 | 4 | 37 | **38** | 41 | |
| | **2** | 6 | 16 | 3 | **7** | 1 | 9 | |
| | **1** | 8 | 41 | **15** | 13 | | 2 | |
| | **0.5** | 4 | **7** | | | | | |
| | **<=0.25** | **17** | 13 | | | | 1 | |
| | | **0.25** | **0.5** | **1** | **2** | **4** | **8** | **>=16** |
| | | **Broth microdilution (BMD) MIC mg/L** | | | | | | |

**Table 3. Overalll MEM categorical agreement between BMD and Vitek2.**

| MIC | ME (*n*, %) | mE (*n*, %) | No error (*n*, %) |
|---|---|---|---|
| **0.25** | 21 (**4**) | 4 (**<1**) | 35 (**6**) |
| **0.5** | 1 (**<1**) | 15 (**3**) | 77 (**14**) |
| **1** | 78 (**14**) | 4 (**<1**) | 18 (**3**) |
| **2** | 40 (**7**) | 39 (**7**) | 20 (**4**) |
| **4** | | 1 (**<1**) | 46 (**8**) |
| **8** | | 32 (**6**) | 48 (**9**) |
| **>=16** | | | 80 (**14**) |
| | 140 (**25**) | 95 (**17**) | 324 (**58**) |

## *Conclusions*

In conclusion, VITEK2 overestimates the MIC to MEM, particularly for strains with class A and class B carbapenemases and therefore overcalls resistance. This may discourage the appropriate use of MEM, alone or in combination with other antibiotics, in the treatment of infections caused by *Enterobacteriaceae* that are clinically susceptible to MEM.

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