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# In-vitro activity of meropenem-vaborbactam against KPC-producing Enterobacteriaceae from Europe collected in 2014-2015

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**Background:** Vaborbactam (formerly RPX7009) is a novel β-lactamase inhibitor with potent activity against class A carbapenemases such as KPC. The meropenem-vaborbactam combination has completed Phase 3 clinical trial for the treatment of complicated urinary tract infections and is being investigated in patients with suspected or documented carbapenem-resistant Enterobacteriaceae (CRE) infections in comparison to best available therapy. The activity of meropenem-vaborbactam and comparator agents was evaluated against a recent European collection of KPC-producing *Enterobacteriaceae*.

**Material/methods:** MICs of meropenem alone or with vaborbactam at a fixed concentration of 8 mg/L, tigecycline, polymyxin B, and gentamicin were determined against 496 KPC-producing, OXA-48- and MBL-negative isolates following CLSI guidelines. The study collection was comprised of 6 species (n): *Klebsiella pneumoniae* (475), *Escherichia coli* (12), *K. oxytoca* (3), *Enterobacter cloacae* (3), *E. aerogenes* (2) and *Citrobacter freundii* (1) and three major KPC variants (n), KPC-2 (242), KPC-3 (252) and KPC-9 (2), collected in 2014-2015 in 12 European countries.

**Results:** Cumulative % inhibited by meropenem (MEM) alone or with vaborbactam (VAB) is shown in the table below, with $MIC_{90}$ values boxed and shaded. $MIC_{50}/_{90}$ values for all strains for meropenem-vaborbactam, tigecycline, polymyxin B, and gentamicin were 0.25/1, 1/2, 0.5/16 and 1/64 mg/L.

| Genotype | | MIC (mg/L) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| (n) | | ≤0.03 | 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | 16 | 32 | >32 |
| All | MEM | | | | | | | 0.8 | 4.0 | 15.3 | 27.0 | 39.1 | **100** |
| (496) | MEM-VAB | 36.3 | 41.7 | 47.4 | 64.3 | 83.7 | **93.1** | 97.2 | 98.8 | 99.2 | 99.6 | | 100 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| KPC-2 | MEM | | | | | | | | 3.3 | 14.9 | 27.7 | 42.6 | **100** |
| (242) | MEM-VAB | 37.2 | 45.9 | 50.4 | 62.4 | 82.2 | **92.1** | 97.5 | 99.2 | 99.6 | 99.6 | | 100 |
| KPC-3 | MEM | | | | | | | 1.6 | 4.8 | 15.9 | 26.6 | 36.1 | **100** |
| (252) | MEM-VAB | 35.7 | 38.1 | 44.8 | 66.7 | 84.9 | **94.0** | 96.8 | 98.4 | 98.8 | 99.6 | | 100 |
| KPC-9 | MEM | | | | | | | | | | | | **100** |
| (2) | MEM-VAB | | | | | **100** | | | | | | | |
| KPC; ESBL pos | MEM | | | | | | | 0.6 | 3.8 | 13.3 | 22.2 | 34.0 | **100** |
| (158) | MEM-VAB | 43.0 | 53.8 | 56.3 | 66.5 | 86.7 | **95.6** | 98.7 | 99.4 | | | | 100 |
| KPC; ESBL neg | MEM | | | | | | | 1.3 | 4.4 | 19.6 | 37.3 | 50.0 | **100** |
| (338) | MEM-VAB | 33.1 | 36.1 | 43.2 | 63.3 | 82.2 | **92.0** | 96.4 | 98.5 | 99.1 | 99.7 | | 100 |

**Conclusions:** Meropenem-vaborbactam showed excellent *in vitro* activity against KPC-producing *Enterobacteriaceae* from Europe, lowering the meropenem $MIC_{50}$ and $MIC_{90}$ from >32 to 0.25 mg/L, and >32 to 1 mg/L, respectively. KPC-type or additional ESBLs do not have impact on the activity of meropenem-vaborbactam. Vaborbactam restores the *in vitro* activity of meropenem against this large collection of recent clinical isolates of KPC-producing *Enterobacteriaceae*.