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# Activity of meropenem/vaborbactam and comparators against Gram-negative isolates from Eastern and Western European patients hospitalized with pneumonia including ventilator-associated pneumonia (2014–19)

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**Objectives:** Meropenem/vaborbactam has been approved in Europe for the treatment of hospital-acquired bacterial pneumonia, ventilator-associated pneumonia (VAP) and bacteraemia among other indications. Vaborbactam is an inhibitor of class A and C β-lactamases, including *Klebsiella pneumoniae* carbapenemase (KPC) enzymes, but not class B or D carbapenemases. We analysed the activity of meropenem/vaborbactam and comparators against 6846 Enterobacterales and 3567 *Pseudomonas aeruginosa* isolates from patients hospitalized with pneumonia (PHP), including VAP.

**Methods:** Isolates from PHP were consecutively collected during 2014–19 from 42 European hospitals located in 21 countries and susceptibility tested using the broth microdilution method. Carbapenem-resistant Enterobacterales (CRE) isolates were molecularly characterized to identify their carbapenem-resistance mechanisms. EUCAST (2020) interpretive criteria were used.

**Results:** The most common Gram-negative pathogens isolated from PHP were *P. aeruginosa* ($n = 3567$), *K. pneumoniae* ($n = 1877$) and *Escherichia coli* ($n = 1646$). Overall, 98.0% of Enterobacterales and 82.1% of *P. aeruginosa* were susceptible to meropenem/vaborbactam, with 99.8% of Enterobacterales and 89.7% of *P. aeruginosa* in Western Europe (WE) and 92.7% of Enterobacterales and 69.1% of *P. aeruginosa* in Eastern Europe (EE). CRE were more common in EE (15.1%) than WE (2.1%). KPC was the most common carbapenemase in WE, while OXA-48-like was the most common carbapenemase in EE. Meropenem/vaborbactam susceptibility was 63.0% for all CRE (92.2% in WE and 51.5% in EE). Meropenem/vaborbactam inhibited 99.1% of KPC-producing isolates and 40.5% of OXA-48-like-producing isolates.

**Conclusions:** These *in vitro* data demonstrate that meropenem/vaborbactam has potent activity against isolates from PHP, including isolates producing KPC, and may be a useful treatment option for PHP, including VAP.

## Introduction

Pneumonia in hospitalized patients, particularly ventilator-associated pneumonia (VAP), is a serious infection that can present treatment challenges and often results in increased mortality.[1,2] Accordingly, carbapenem-resistant Enterobacterales (CRE) isolates are a growing global concern. Among carbapenemases detected in Enterobacterales species, *Klebsiella pneumoniae* carbapenemases (KPCs) have disseminated worldwide and are now endemic in many hospitals across a wide range of countries.

Meropenem/vaborbactam, ceftazidime/avibactam and imipenem/relebactam are new inhibitor combinations that are active against specific types of carbapenemases and have been approved in the USA and Europe.[3] Vaborbactam is a cyclic boronic acid β-lactamase inhibitor that was developed to inhibit Ambler class A enzymes, including KPC, and class C β-lactamases. When combined with meropenem, vaborbactam restored the activity of this carbapenem against KPC-producing isolates in comparison with meropenem alone. Vaborbactam, like other currently approved inhibitors, has no activity against class B MBLs.[4–6] Vaborbactam has less inhibitory activity against class D carbapenemases (OXA-48) than class A enzymes.

Meropenem/vaborbactam is approved in Europe for the treatment of: complicated urinary tract infections, including acute

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pyelonephritis; complicated intra-abdominal infections; hospital-acquired bacterial pneumonia, including VAP; bacteraemia that occurs with any of the previously mentioned infections; and infections due to aerobic Gram-negative organisms in adults with limited treatment options.[7]

In this study, we evaluated the activity of meropenem/vaborbactam and comparators against Enterobacterales and *Pseudomonas aeruginosa* isolates from patients hospitalized with pneumonia (PHP), including VAP, in European hospitals from 2014 to 2019 as part of the SENTRY Antimicrobial Surveillance Program.[8]

## Materials and methods

### Study design

A total of 10 413 Gram-negative isolates (6846 Enterobacterales and 3567 *P. aeruginosa*) were collected from PHP in 42 European hospitals across 21 countries (1–6 hospitals per country) as previously described.[9] Isolates were consecutively collected; one isolate per patient per infection episode was submitted.

Isolates were susceptibility tested using broth microdilution methods according to CLSI standards.[10] EUCAST interpretive criteria were used.[11] The EUCAST susceptible breakpoint for meropenem/vaborbactam of ≤8 mg/L reflected the higher standard dose of the meropenem component and the inhibitory activity of vaborbactam, compared with the standard dose of meropenem alone, which has a susceptible breakpoint of ≤2 mg/L. The EUCAST Enterobacterales breakpoints for imipenem tested against *Proteus* spp., *Providencia* spp. and *Morganella morganii* and the *P. aeruginosa* breakpoints for piperacillin/tazobactam, cefepime, ceftazidime, imipenem, aztreonam and ciprofloxacin were updated to recategorize all isolates previously considered susceptible to these agents as 'susceptible, increased exposure (intermediate)'.[11]

### CRE

Enterobacterales isolates that had MICs of meropenem, doripenem and/or imipenem (imipenem was not used for *Proteus* spp., *Providencia* spp. or *M. morganii*) >2 mg/L were analysed for the presence of carbapenemases by PCR (2014–15) or WGS (2016–19), as previously described.[12,13]

MDR *P. aeruginosa* were non-susceptible to at least one agent in three or more antimicrobial classes, as described by Magiorakos *et al.*[14]

### Subset analyses

Susceptibilities were analysed by European region: 3034 isolates were from the Eastern European countries of Belarus, the Czech Republic, Greece, Israel, Hungary, Poland, Romania, Russia, Slovenia, Turkey and Ukraine; and, for Western Europe, 7379 isolates were from Austria, Belgium, Denmark, Finland, France, Germany, Ireland, Italy, Portugal, Spain, Sweden, Switzerland and the UK. Due to the limited number of sites in each country, this study was not designed to determine the overall prevalence of carbapenemases in participating countries.

## Results

### Organisms

The most common Gram-negative species isolated from pneumonia in hospitalized patients was *P. aeruginosa* ($n = 3567$). The most common Enterobacterales species isolated were *K. pneumoniae* ($n = 1877$) and *Escherichia coli* ($n = 1646$).

### Susceptibilities

#### *Enterobacterales*

The susceptibilities to meropenem/vaborbactam and comparators tested against isolates from patients with pneumonia caused by Enterobacterales or *P. aeruginosa* and resistance groups are shown in Table 1. The overall susceptibility of Enterobacterales to meropenem/vaborbactam was 98.0%, the highest among the tested drugs. The susceptibility to meropenem/vaborbactam was higher in Western Europe than Eastern Europe, at 99.8% and 92.7%, respectively. Meropenem susceptibility was 95.1% overall (86.1% in Eastern Europe and 98.1% in Western Europe). Susceptibilities to the comparators were also higher in Western Europe than in Eastern Europe.

#### *CRE*

There were 362 CRE (362/6846, 5.3%) (Table 1). The majority of CRE were *K. pneumoniae* (89.2% 323/362). The most common carbapenemases were KPC ($n = 114$) and OXA-48-like ($n = 116$). Italy had the highest number of KPC-producing isolates at 59 (51.3%). KPC-producing isolates were mainly *K. pneumoniae* ($n = 109$), which included 71 $bla_{KPC-3}$, 37 $bla_{KPC-2}$ and 1 $bla_{KPC-12}$. Four *E. coli* had $bla_{KPC-3}$ and one *Enterobacter cloacae* species complex had a $bla_{KPC-2}$. The MBLs identified were 19 $bla_{VIM-like}$ and 59 $bla_{NDM-1}$. There were 54 CRE isolates (45 *K. pneumoniae*, 5 *Klebsiella aerogenes*, 2 *E. cloacae* species complex and 2 *Serratia marcescens*) that were negative for recognized carbapenemase genes. Of these CRE isolates, 43 (including 39 *K. pneumoniae*) were from Poland.

Meropenem/vaborbactam was the most potent agent tested against KPC-producing isolates, as it inhibited 99.1% of 114 isolates (Table 1). Meropenem/vaborbactam had less activity against isolates producing class B or D carbapenemases; 40.5% of 116 isolates producing OXA-48-like enzymes were susceptible to meropenem/vaborbactam, while 13.8% were susceptible to meropenem alone (data not shown). Only 1.7% of 59 isolates producing NDM-1 were susceptible to meropenem/vaborbactam (data not shown). Nineteen isolates produced VIM-like enzymes; 15 (78.9%) of these isolates were susceptible to meropenem/vaborbactam and 5 (26.3%) were susceptible to meropenem alone. Fifty-one of 54 (96.3%) isolates that were CRE but did not contain a carbapenemase were susceptible to meropenem/vaborbactam and 5 (9.3%) were susceptible to meropenem.

#### *P. aeruginosa*

Meropenem/vaborbactam susceptibility was 82.1% overall, 69.2% in Eastern Europe and 89.7% in Western Europe (Table 1). Meropenem susceptibility was 67.3% overall, 49.7% in Eastern Europe and 77.5% in Western Europe. The carbapenem-resistant *P. aeruginosa* were not genetically characterized. Twenty-seven percent of *P. aeruginosa* were MDR, meropenem/vaborbactam susceptibility was 41.0% (31.5% in Eastern Europe and 53.0% in Western Europe) and susceptibility to meropenem alone was 13.0% (8.3% in Eastern Europe and 18.8% in Western Europe) (Table 1).

**Table 1.** Antimicrobial activity of meropenem/vaborbactam and comparator agents tested against organisms/organism groups

| Organism/antimicrobial agent | $MIC_{50}$ (mg/L) | $MIC_{90}$ (mg/L) | Percentage susceptible (%S)/percentage resistant (%R) using EUCAST criteria[a] | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Europe | | Eastern Europe | | Western Europe | |
| | | | %S | %R | %S | %R | %S | %R |
| Enterobacterales (*n*) | | | (6846) | | (1724) | | (5122) | |
| meropenem/vaborbactam | 0.03 | 0.06 | 98.0 | 2 | 92.7 | 7.3 | 99.8 | 0.2 |
| meropenem | 0.03 | 0.12 | 95.1 | 3.4 | 86.1 | 9.5 | 98.1 | 1.3 |
| imipenem | 0.25 | 2 | [b] | 3.9 | [b] | 10.3 | [b] | 1.7 |
| amikacin | 2 | 4 | 94.2[c] | 5.8 | 83.1[c] | 16.9 | 97.9[c] | 2.1 |
| aztreonam | ≤0.12 | >16 | 72.9 | 24.4 | 52.5 | 45 | 79.8 | 17.4 |
| cefepime | ≤0.5 | >16 | 77.4 | 18.9 | 53.8 | 42.3 | 85.3 | 11 |
| ceftazidime | 0.25 | >32 | 72.0 | 23.1 | 51.9 | 44.1 | 78.8 | 16 |
| colistin | ≤0.5 | >8 | 76.8 | 23.2 | 80.1 | 19.9 | 75.7 | 24.3 |
| gentamicin | ≤1 | >8 | 85.3[c] | 14.7 | 69.2[c] | 30.8 | 90.7[c] | 9.3 |
| levofloxacin | ≤0.12 | >4 | 75.0 | 21.9 | 55.4 | 40.6 | 81.5 | 15.6 |
| piperacillin/tazobactam | 2 | >64 | 75.6 | 19.4 | 59.8 | 34.2 | 80.9 | 14.4 |
| CRE (*n*) | | | (362) | | (260) | | (102) | |
| meropenem/vaborbactam | 4 | >32 | 63.0 | 37.0 | 51.5 | 48.5 | 92.2 | 7.8 |
| meropenem | 16 | >32 | 7.7 | 63.5 | 8.1 | 63.1 | 6.9 | 64.7 |
| imipenem | 8 | >8 | [b] | 71.8 | [b] | 68.1 | [b] | 81.4 |
| amikacin | 16 | >32 | 41.4[c] | 58.6 | 34.2[c] | 65.8 | 59.8[c] | 40.2 |
| aztreonam | >16 | >16 | 8.8 | 90.6 | 10.8 | 88.5 | 3.9 | 96.1 |
| cefepime | >16 | >16 | 4.7 | 90.6 | 5.8 | 90 | 2.0 | 92.2 |
| ceftazidime | >32 | >32 | 6.6 | 92.3 | 8.1 | 90.4 | 2.9 | 97.1 |
| colistin | ≤0.5 | >8 | 74.2 | 25.8 | 72.6 | 27.4 | 78.4 | 21.6 |
| gentamicin | >8 | >8 | 39.8[c] | 60.2 | 34.2[c] | 65.8 | 53.9[c] | 46.1 |
| levofloxacin | >4 | >4 | 8.9 | 88.1 | 6.6 | 90 | 14.7 | 83.3 |
| piperacillin/tazobactam | >64 | >64 | 0.3 | 99.4 | 0.4 | 99.6 | 0 | 99 |
| KPC-producing CRE (*n*) | | | (114) | | (40) | | (74) | |
| meropenem/vaborbactam | 0.12 | 1 | 99.1 | 0.9 | 97.5 | 2.5 | 100 | 0 |
| meropenem | 32 | >32 | 1.8 | 75.4 | 5.0 | 75 | 0 | 75.7 |
| imipenem | >8 | >8 | 3.5 | 92.1 | 10.0 | 87.5 | 0 | 94.6 |
| amikacin | 16 | >32 | 43.0[c] | 57 | 22.5[c] | 77.5 | 54.1[c] | 45.9 |
| aztreonam | >16 | >16 | 0 | 100.0 | 0 | 100.0 | 0 | 100.0 |
| cefepime | >16 | >16 | 0 | 99.1 | 0 | 100.0 | 0 | 98.6 |
| ceftazidime | >32 | >32 | 0 | 100.0 | 0 | 100.0 | 0 | 100.0 |
| colistin | ≤0.5 | >8 | 72.8 | 27.2 | 62.5 | 37.5 | 78.4 | 21.6 |
| gentamicin | 2 | >8 | 59.6[c] | 40.4 | 65.0[c] | 35 | 56.8[c] | 43.2 |
| levofloxacin | >4 | >4 | 4.4 | 94.7 | 0 | 97.5 | 6.8 | 93.2 |
| piperacillin/tazobactam | >64 | >64 | 0 | 99.1 | 0 | 100.0 | 0 | 98.6 |
| *P. aeruginosa* (*n*) | | | (3567) | | (1310) | | (2257) | |
| meropenem/vaborbactam | 0.5 | 32 | 82.1 | 17.9 | 69.2 | 30.8 | 89.7 | 10.3 |
| meropenem | 0.5 | 32 | 67.3 | 17.8 | 49.7 | 30.3 | 77.5 | 10.6 |
| imipenem | 1 | >8 | [b] | 31.1 | [b] | 48.9 | [b] | 20.8 |
| amikacin | 4 | >32 | 86.0[c] | 14 | 72.8[c] | 27.2 | 93.7[c] | 6.3 |
| aztreonam | 8 | >16 | [b] | 22.5 | [b] | 26.4 | [b] | 20.2 |
| cefepime | 4 | 16 | [b] | 23.7 | [b] | 33.8 | [b] | 17.8 |
| ceftazidime | 2 | >32 | [b] | 27 | [b] | 37.4 | [b] | 21 |
| colistin | 1 | 2 | 99.4 | 0.6 | 99.1 | 0.9 | 99.6 | 0.4 |
| gentamicin | 2 | >8 | | | | | | |
| levofloxacin | 1 | >4 | [b] | 42 | [b] | 57.2 | [b] | 33.2 |
| piperacillin/tazobactam | 8 | >64 | [b] | 30.6 | [b] | 40.9 | [b] | 24.5 |
| MDR *P. aeruginosa* (*n*) | | | (972) | | (542) | | (430) | |
| meropenem/vaborbactam | 16 | >32 | 41.0 | 59.0 | 31.5 | 68.5 | 53.0 | 47.0 |

*Continued*

**Table 1.** *Continued*

| Organism/antimicrobial agent | $MIC_{50}$ (mg/L) | $MIC_{90}$ (mg/L) | Percentage susceptible (%S)/percentage resistant (%R) using EUCAST criteria[a] | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Europe | | Eastern Europe | | Western Europe | |
| | | | %S | %R | %S | %R | %S | %R |
| meropenem | 16 | >32 | 13.0 | 59.5 | 8.3 | 67.9 | 18.8 | 48.8 |
| imipenem | >8 | >8 | [b] | 79.8 | [b] | 87.8 | [b] | 69.8 |
| amikacin | 16 | >32 | 53.1[c] | 46.9 | 38.6[c] | 61.4 | 71.4[c] | 28.6 |
| aztreonam | >16 | >16 | [b] | 55.5 | [b] | 48.3 | [b] | 64.4 |
| cefepime | 16 | >16 | [b] | 76.4 | [b] | 78 | [b] | 74.4 |
| ceftazidime | 32 | >32 | [b] | 82 | [b] | 83 | [b] | 80.7 |
| colistin | 1 | 2 | 99.0 | 1.0 | 98.7 | 1.3 | 99.3 | 0.7 |
| gentamicin | >8 | >8 | | | | | | |
| levofloxacin | >4 | >4 | [b] | 90.9 | [b] | 94.6 | [b] | 86.3 |
| piperacillin/tazobactam | 64 | >64 | [b] | 93.3 | [b] | 91.7 | [b] | 95.3 |

[a]Criteria as published by EUCAST.[11]
[b]An arbitrary susceptible breakpoint of ≤0.001 mg/L and/or >50 mm has been published by EUCAST indicating that susceptible should not be reported for this organism/agent combination and intermediate should be interpreted as 'susceptible increased exposure'.[11] For imipenem with Enterobacterales, this decision applies to *M. morganii, Proteus* spp. and *Providencia* spp.
[c]For infections originating from the urinary tract. For systemic infections, aminoglycosides must be used in combination with another active therapy.

### *Susceptibilities of ICU and ICU-VAP isolates*

The susceptibilities to meropenem/vaborbactam and comparators for Enterobacterales and *P. aeruginosa* are shown stratified in Table 2 for isolates from ICU patients with pneumonia and the subset of isolates from ICU patients with VAP from Eastern and Western Europe.

For Enterobacterales isolates from ICU patients and ICU patients with VAP, meropenem/vaborbactam was the most active agent tested. The susceptibilities of ICU isolates and of ICU-VAP isolates to meropenem/vaborbactam were similar (97.1% and 96.7% respectively). Susceptibilities to meropenem alone were 94.1% for all ICU isolates and 93.2% for ICU-VAP isolates.

The susceptibility to meropenem/vaborbactam for *P. aeruginosa* isolates from ICU patients was 73.2% and meropenem susceptibility was 57.0% (Table 2). The susceptibility to meropenem/vaborbactam for *P. aeruginosa* isolates from ICU patients with VAP was 67.6% and meropenem susceptibility was 51.3%.

## Discussion

To the best of our knowledge, this is the first study on the activity of meropenem/vaborbactam against a large collection of Enterobacterales and *P. aeruginosa* isolates from PHP in Europe. Meropenem/vaborbactam had the highest susceptibility (98.0%) of tested agents against Enterobacterales isolates. Against *P. aeruginosa*, meropenem/vaborbactam was the most active β-lactam tested (82.1% susceptible), with amikacin (86.0%) and colistin (99.4%) having higher susceptibilities. This study expands on the previous global studies with Enterobacterales isolates from multiple infection types.[12,15] In the current study of pneumonia isolates, we found that the susceptibilities of both Enterobacterales and *P. aeruginosa* varied between Eastern and Western European countries, with generally lower susceptibilities in Eastern Europe. Although large multinational surveillance programmes vary in design, the higher resistance rates in Eastern Europe compared with Western Europe are consistent with results from the EARS-Net programme.[16,17] Recently, a similar study was published on meropenem/vaborbactam tested against pneumonia isolates from US patients.[9] The meropenem/vaborbactam susceptibility of US isolates was comparable to that of Western European isolates, reflecting the prevalence of KPC as the primary carbapenemase in these regions.

We examined the activity of meropenem/vaborbactam against CRE, including characterized carbapenemase-producing isolates. The distribution of carbapenemases was quite different between European regions, with KPC as the predominate carbapenemase in Western Europe, particularly in Italy, while Eastern European countries had greater numbers of MBLs and OXA-48-like carbapenemases. Meropenem/vaborbactam inhibited nearly all KPC-expressing isolates but had less activity against MBL-producing and OXA-48-producing isolates.

Isolates that were CRE but did not contain a carbapenemase were most common in Poland (43/54, 79.6%). Possible resistance mechanisms include porin alterations or disruptions and/or efflux pump up-regulation.[13,18] Almost all (51/54, 96.3%) were susceptible to meropenem/vaborbactam. These isolates were not characterized further in this study, but will be in future studies.

Study limitations include that the carbapenem-resistant *P. aeruginosa* were not genetically characterized, the number of sites per country were limited, this study was not designed to be indicative of the overall carbapenem-resistance rates in each country and, finally, one or more institutions may have had an outbreak during the surveillance period that could have impacted resistance rates.

**Table 2.** Susceptibilities of ICU and ICU-VAP isolates to meropenem/vaborbactam and comparators

| Organism/antimicrobial agent | $MIC_{50}$ (mg/L) | $MIC_{90}$ (mg/L) | Percentage susceptible (%S)/percentage resistant (%R) using EUCAST criteria[a] | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Europe | | Eastern Europe | | Western Europe | |
| | | | %S | %R | %S | %R | %S | %R |
| Enterobacterales | | | | | | | | |
| ICU (*n*) | | | (3169) | | (1010) | | (2159) | |
| meropenem/vaborbactam | 0.03 | 0.12 | 97.1 | 2.9 | 91.1 | 8.9 | 99.9 | 0.1 |
| meropenem | 0.03 | 0.12 | 94.1 | 4.1 | 84.8 | 10.6 | 98.5 | 1.1 |
| imipenem | 0.25 | 2 | [b] | 4.3 | [b] | 10.5 | [b] | 1.3 |
| amikacin | 2 | 8 | 92.9[c] | 7.1 | 81.0[c] | 19 | 98.5[c] | 1.5 |
| aztreonam | ≤0.12 | >16 | 70.4 | 27.4 | 47.9 | 49.7 | 80.9 | 17 |
| cefepime | ≤0.5 | >16 | 75.2 | 21.3 | 48.5 | 47.4 | 87.6 | 9.1 |
| ceftazidime | 0.25 | >32 | 69.5 | 26.1 | 47.4 | 48.2 | 79.8 | 15.7 |
| colistin | ≤0.5 | >8 | 76.8 | 23.2 | 79.2 | 20.8 | 75.7 | 24.3 |
| gentamicin | ≤1 | >8 | 84.4[c] | 15.6 | 65.7[c] | 34.3 | 93.2[c] | 6.8 |
| levofloxacin | ≤0.12 | >4 | 75.8 | 21.6 | 52.9 | 42.7 | 86.5 | 11.7 |
| piperacillin/tazobactam | 2 | >64 | 72.9 | 22.2 | 55.4 | 38.7 | 81 | 14.5 |
| ICU-VAP (*n*) | | | (1890) | | (735) | | (1155) | |
| meropenem/vaborbactam | 0.03 | 0.25 | 96.7 | 3.3 | 91.6 | 8.4 | 99.9 | 0.1 |
| meropenem | 0.03 | 0.5 | 93.2 | 4.3 | 83.9 | 10.2 | 99.1 | 0.6 |
| imipenem | 0.25 | 2 | [b] | 4.6 | [b] | 10.9 | [b] | 0.6 |
| amikacin | 2 | 8 | 91.5[c] | 8.5 | 79.0[c] | 21 | 99.4[c] | 0.6 |
| aztreonam | ≤0.12 | >16 | 68.2 | 29.8 | 44.8 | 53.1 | 83 | 14.9 |
| cefepime | ≤0.5 | >16 | 72.6 | 24 | 44.9 | 51.2 | 90.2 | 6.7 |
| ceftazidime | 0.25 | >32 | 67.4 | 28.3 | 44.2 | 51 | 82.2 | 13.9 |
| colistin | ≤0.5 | >8 | 76.8 | 23.2 | 80.4 | 19.6 | 74.5 | 25.5 |
| gentamicin | ≤1 | >8 | 82.6[c] | 17.4 | 64.1[c] | 35.9 | 94.4[c] | 5.6 |
| levofloxacin | ≤0.12 | >4 | 74.3 | 23.1 | 49.6 | 46.2 | 90 | 8.4 |
| piperacillin/tazobactam | 2 | >64 | 70.9 | 24.1 | 53.5 | 41.6 | 82 | 13 |
| *P. aeruginosa* | | | | | | | | |
| ICU (*n*) | | | (1422) | | (679) | | (743) | |
| meropenem/vaborbactam | 1 | >32 | 73.2 | 26.8 | 58.8 | 41.2 | 86.4 | 13.6 |
| meropenem | 1 | >32 | 57 | 26.1 | 40.4 | 40.2 | 72.3 | 13.2 |
| imipenem | 2 | >8 | [b] | 41.6 | [b] | 59.2 | [b] | 25.4 |
| amikacin | 4 | >32 | 81.5[c] | 18.5 | 68.1[c] | 31.9 | 93.7[c] | 6.3 |
| aztreonam | 8 | >16 | [b] | 27.9 | [b] | 30.8 | [b] | 25.3 |
| cefepime | 4 | >16 | [b] | 31.1 | [b] | 40.8 | [b] | 22.2 |
| ceftazidime | 4 | >32 | [b] | 35.1 | [b] | 44.5 | [b] | 26.5 |
| colistin | 1 | 2 | 99.5 | 0.5 | 99.3 | 0.7 | 99.7 | 0.3 |
| gentamicin | 2 | >8 | | | | | | |
| levofloxacin | 1 | >4 | [b] | 45.2 | [b] | 60.3 | [b] | 31.4 |
| piperacillin/tazobactam | 8 | >64 | [b] | 38.8 | [b] | 48.4 | [b] | 30.1 |
| ICU-VAP (*n*) | | | (910) | | (552) | | (358) | |
| meropenem/vaborbactam | 2 | >32 | 67.6 | 32.4 | 54.2 | 45.8 | 88.3 | 11.7 |
| meropenem | 2 | >32 | 51.3 | 31.5 | 36.4 | 44.9 | 74.3 | 10.9 |
| imipenem | 4 | >8 | [b] | 48.1 | [b] | 64.1 | [b] | 23.5 |
| amikacin | 4 | >32 | 75.8[c] | 24.2 | 63.9[c] | 36.1 | 94.1[c] | 5.9 |
| aztreonam | 8 | >16 | [b] | 30.3 | [b] | 32.2 | [b] | 27.4 |
| cefepime | 8 | >16 | [b] | 35.2 | [b] | 43.8 | [b] | 21.8 |
| ceftazidime | 4 | >32 | [b] | 39.6 | [b] | 46.9 | [b] | 28.2 |
| colistin | 1 | 2 | 99.6 | 0.4 | 99.5 | 0.5 | 99.7 | 0.3 |
| gentamicin | 2 | >8 | | | | | | |
| levofloxacin | 2 | >4 | [b] | 53 | [b] | 64.1 | [b] | 36 |
| piperacillin/tazobactam | 16 | >64 | [b] | 44.1 | [b] | 51.9 | [b] | 32.1 |

[a]Criteria as published by EUCAST.[11]

[b]An arbitrary susceptible breakpoint of ≤0.001 mg/L and/or >50 mm has been published by EUCAST indicating that susceptible should not be reported for this organism/agent combination and intermediate should be interpreted as 'susceptible increased exposure'.[11] For imipenem with Enterobacterales, this decision applies to *M. morganii, Proteus* spp. and *Providencia* spp.

[c]For infections originating from the urinary tract. For systemic infections, aminoglycosides must be used in combination with another active therapy.

These *in vitro* data suggest that meropenem/vaborbactam may be a useful treatment option for both ICU and non-ICU PHP, including VAP, caused by Enterobacterales or *P. aeruginosa*, even when pneumonia is caused by CRE in regions with a high prevalence of KPCs.

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## Transparency declarations

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