# Activity of Meropenem-Vaborbactam and Comparators Against European Carbapenem-Resistant Enterobacterales Isolates Producing KPC Carbapenemase (2018-2020)

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## Objective

Meropenem-vaborbactam (MVB) is a combination of a carbapenem, and a carbapenemase inhibitor developed to inhibit Class A and C beta-lactamases, including the common *Klebsiella pneumoniae* carbapenemase (KPC).

MVB was approved by the European Medicines Agency for the treatment of complicated urinary tract infections (cUTI), including acute pyelonephritis, complicated intra-abdominal infections (cIAI), hospital-acquired bacterial pneumonia, ventilator-associated pneumonia, and bacteremia (BSI) associated with any of the infections listed above.

The objective of this study was to analyse the activity of MVB and comparators against KPC-producing carbapenem-resistant Enterobacterales (CRE) collected in European hospitals from 2018 to 2020 as part of the SENTRY Antimicrobial Surveillance Program.

## Methods

- A total of 16,866 Enterobacterales clinical isolates were consecutively collected from hospitalized patients in 39 sites from 19 European countries.
- Susceptibility testing was performed using the CLSI broth microdilution method. EUCAST (2022) interpretive criteria were used.
- All infection types were included (Figure 1).
- 679 CRE were identified as having an MIC >2 mg/L to meropenem and/or imipenem. Whole genome sequencing was performed on each CRE isolate; 227 isolates contained *bla*$_{KPC}$.
  - 226/227 isolates with *bla*$_{KPC}$ also contained 1-6 additional beta-lactamase enzymes including various *bla*$_{TEM}$, *bla*$_{SHV}$ and *bla*$_{CTX-M.}$ 6 isolates also contained a metallo-beta-lactamase, *bla*$_{VIM-1}$ or *bla*$_{NDM-1.}$
  - Species containing *bla*$_{KPC}$: *Citrobacter freundii* species complex (1), *Enterobacter cloacae* species complex (2), *Escherichia coli* (6), and *Klebsiella pneumoniae* (218).

# Results

Figure 1. KPC-Producing Isolates by Infection Type

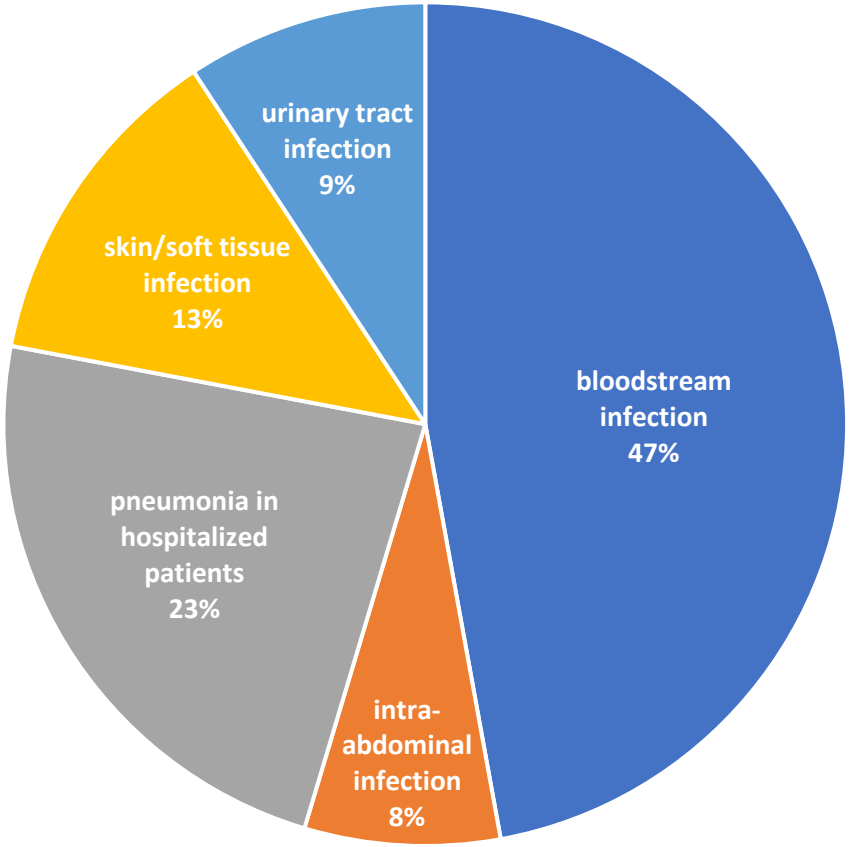
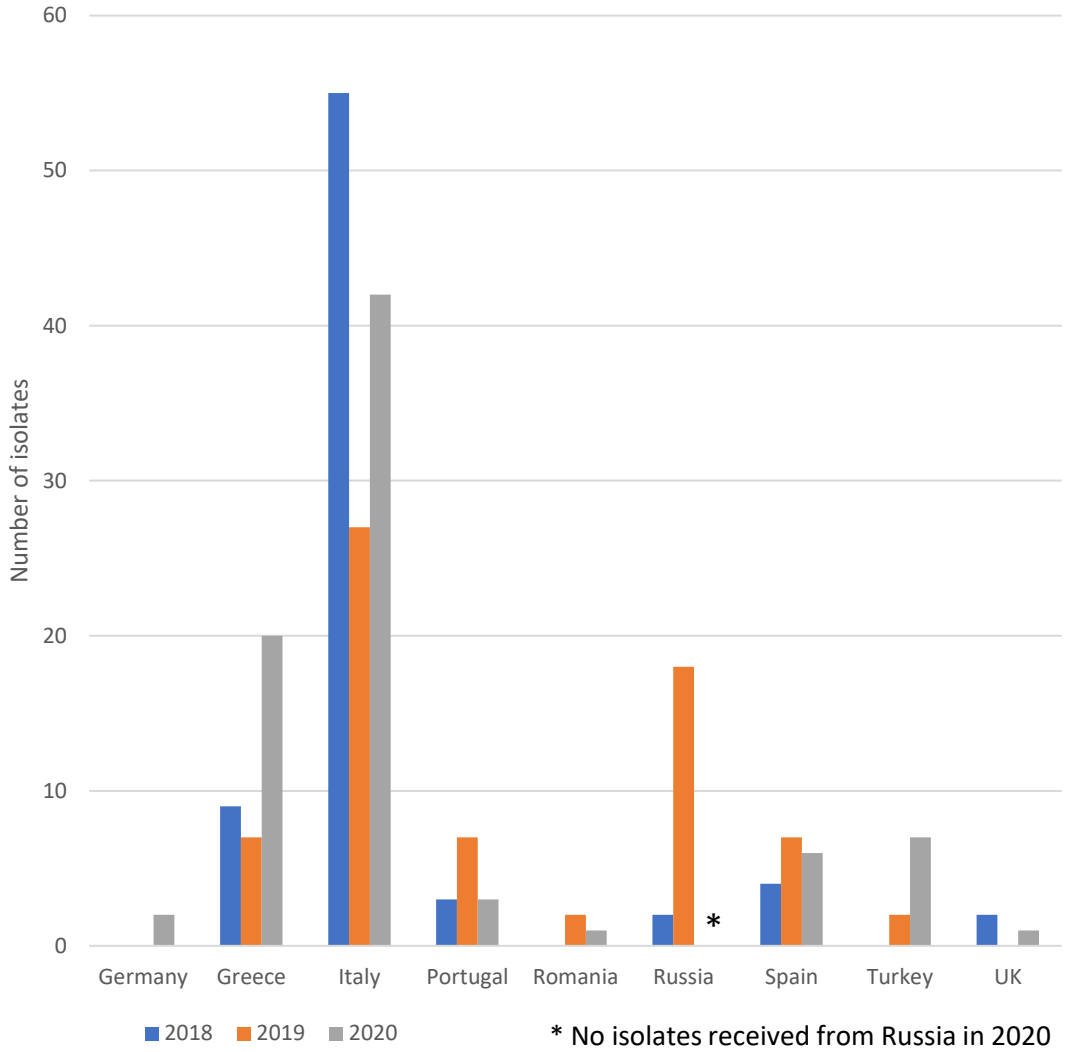



Figure 2. KPC-Producing Isolates by Country and Year




* No isolates received from Russia in 2020

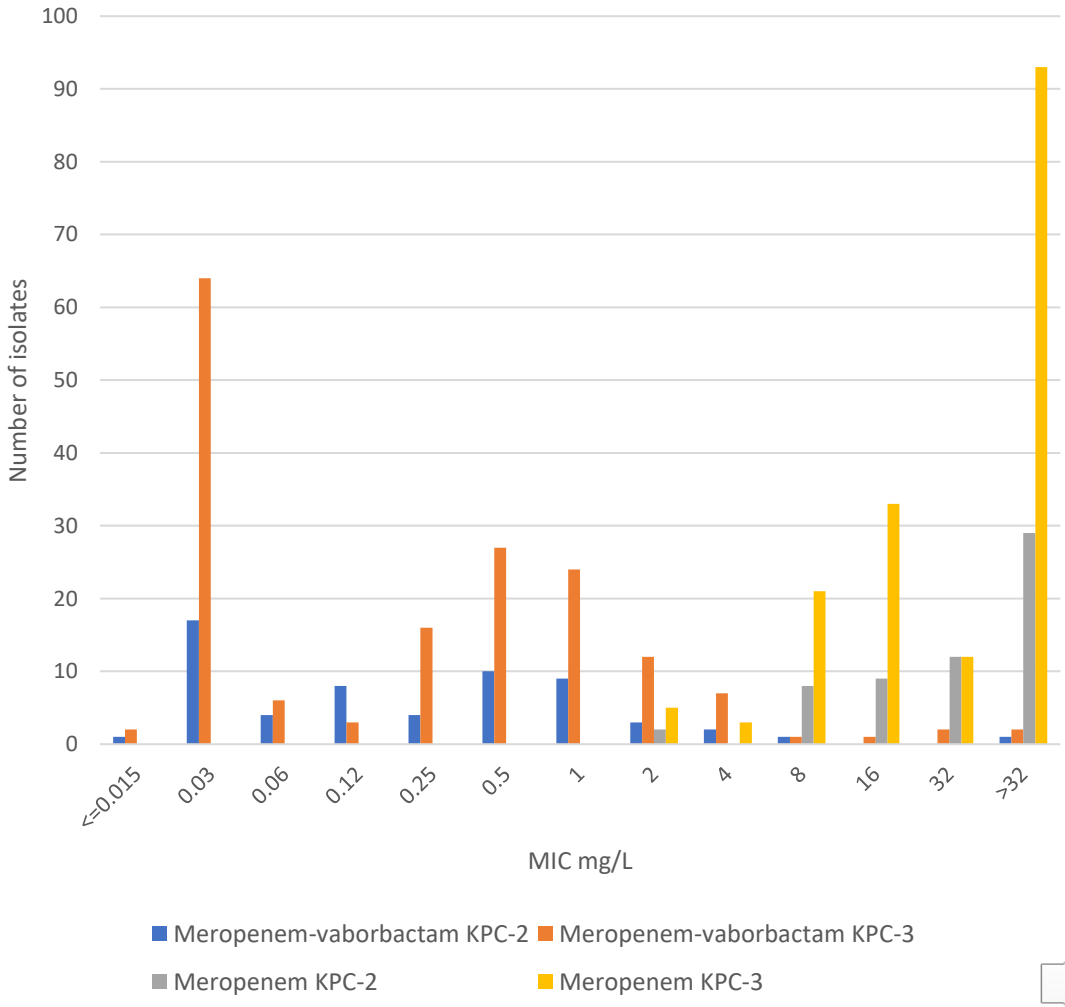
# Results

## Table 1. Activity of Meropenem-vaborbactam and Comparator Antimicrobial Agents Tested Against 227 KPC-producing European Isolates (2018-2020)

| Antimicrobial agent | mg/L | | EUCAST[a] | | |
|---|---|---|---|---|---|
| | $MIC_{50}$ | $MIC_{90}$ | %S | %I | %R |
| Meropenem-vaborbactam | 0.25 | 2 | 97.4 | | 2.6 |
| Meropenem | >32 | >32 | 3.1 [b]<br>3.1 [c] | <br>14.1 | 96.9<br>82.8 |
| Imipenem | >8 | >8 | 0.0 | 3.5 | 96.5 |
| Amikacin | 8 | >32 | 50.2 [d] | | 49.8 |
| Aztreonam | >16 | >16 | 0.0 | 0.0 | 100.0 |
| Cefepime | >32 | >32 | 0.4 | 0.4 | 99.1 |
| Ceftazidime | >32 | >32 | 0.0 | 0.4 | 99.6 |
| Colistin | 0.25 | >8 | 83.7 | | 16.3 |
| Gentamicin | 2 | >16 | 53.7 [d] | | 46.3 |
| Levofloxacin | >32 | >32 | 6.2 | 0.4 | 93.4 |
| Piperacillin-tazobactam | >128 | >128 | 0.0 | | 100.0 |

[a] Criteria as published by EUCAST (2021).
[b] Using meningitis breakpoints.
[c] Using non-meningitis breakpoints.
[d] For infections originating from the urinary tract. For systemic infections, aminoglycosides must be used in combination with other active therapy.
Organisms include *Citrobacter freundii* species complex (1), *Enterobacter cloacae* species complex (2), *Escherichia coli* (6), and *Klebsiella pneumoniae* (218).

## Figure 3 MIC distributions of KPC 2 & 3 Producing Isolates



## Results

- The most common KPC-producing species were *Klebsiella pneumoniae* (KPN; *n* = 218) and *Escherichia coli* (*n* = 6; Table 1).
  - Bloodstream infections had the most KPC-producing isolates (Figure 1).
- The number of KPC-producing isolates varied by country and year (Figure 2).
- Of the 227 KPC-producing isolates, 167 produced KPC-3 and 60 had KPC-2. MVB activity was similar against both groups (Figure 3).
- The susceptibility to MVB was 97.4%, the highest of the agents tested; meropenem susceptibility was 3.1% (Table 1).
  - 6 MVB-resistant isolates contained both KPC and a metallo-beta lactamase, either VIM-1 or NDM-1.
  - All but 1 isolate also contained other beta-lactamase enzymes, CTX-M-15 (*n* = 71) was the most common extended spectrum beta-lactamase (ESBL).

## Conclusions

- KPC prevalence varied by country.
  - Italy had the highest number of KPCs.
  - The number of KPCs declined in Italy but increased in Greece and Turkey from 2018 to 2020.
- MVB had potent *in vitro* activity against CRE isolates producing KPC and had the highest susceptibility of tested agents.
- These in vitro data suggest that MVB is a useful treatment for infections caused by CRE that produce KPC and ESBLs.


## Acknowledgements

This poster has been funded by A. Menarini Industrie Farmaceutiche Riunite SRL.



## Contact

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