Activity of Meropenem-Vaborbactam and Comparators Against Enterobacteriales Isolates from Patients in Hematology/Oncology and Transplant Units in the United States

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Introduction

Patients undergoing treatment for cancer or receiving an organ transplant are often immunosuppressed and particularly susceptible to infections caused by Gram-negative pathogens, including carbapenem-resistant organisms.

Meropenem-vaborbactam is a combination of a carbapenem and a β-lactam inhibitor that is effective against Class A and C β-lactamases, including KPC carbapenemase, and KPC-producing OXA class D enzymes.

We evaluated the activity of meropenem-vaborbactam and comparators against Enterobacteriales isolates collected worldwide during 2014–2020 from patients in US medical centers as part of the SENTRY Antimicrobial Surveillance Program.

Methods

- A total of 2,185 clinical isolates were consecutively collected from patients in hematology/oncology or transplant units in 20 hospitals in the United States during 2014–2020.
- Of these, 2,185 clinical isolates were selected for susceptibility testing using CLSI M100 (2016) broth microdilution methodology. Results were interpreted using CLSI M100 (2020) breakpoints.
- Enterobacteriales Enterobacterales (CRE) were characterized as having MIC values ≥4 mg/L to imipenem and/or meropenem.
- CRE were genotypically characterized for carbapenemase genes by PCR prior to 2016 or whole genome sequencing (2016–2020), as previously described Castanheira, 2015. Stains in US Census Division
- New England Division: Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island and Vermont
- Middle Atlantic Division: New Jersey, New York and Pennsylvania
- East North Central Division: Illinois, Indiana, Michigan, Ohio and Wisconsin
- West North Central Division: Iowa, Kansas, Minnesota, Missouri, Nebraska, North Dakota and South Dakota
- South Atlantic Division: Delaware, District of Columbia, Florida, Georgia, Maryland, North Carolina, South Carolina, Virginia and West Virginia
- East South Central Division: Alabama, Kentucky, Mississippi and Tennessee
- West South Central Division: Arkansas, Louisiana, Oklahoma and Texas
- Mountain Division: Arizona, Colorado, Idaho, Montana, New Mexico, Utah and Wyoming
- Pacific Division: Hawaii, California, Nevada, Oregon and Washington

Results

- 2,185 isolates were included in the study.
- The most common species isolated were Enterichiria coli (n=858; 39.0%), Klebsiella pneumoniae (n=528; 24.3%), and Enterobacter cloacae species complex (n=500; 23.0%) (Figure 1).
- The most common infection type was bloodstream infection (n=1,477; 67.5%).
- Susceptibility of these isolates to meropenem-vaborbactam was 71.4%.
- Susceptibility of these isolates to imipenem and piperacillin-tazobactam was 25.2% and 0.3%, respectively (Table 1).
- All CRE were genotypically characterized.
- 12 isolates produced KPC.
- 6 isolates were from the Mid-Atlantic Census Division, 4 were from the West North Central Division, and 1 each from the New England, South Atlantic, and Pacific Divisions.
- 1 isolate produced OXA-48, 2 from the Mid Atlantic and 1 from West South Central Division.
- Of these 25 genotypically characterized CRE isolates:
- 2 produced IMP-4, both from the Mid-Atlantic Division
- 3 were negative for known carbapenemase genes, 2 from South Atlantic and 1 from West South Central Division
- All 25 CRE-producing isolates were susceptible to meropenem-vaborbactam.
- All 25 CRE-producing isolates were susceptible to meropenem-vaborbactam.
- Of the 25 CRE-producing isolates tested against Enterobacterales isolates causing infections in patients in the United States:
- 100% of KPC–producing isolates and all 3 of the carbapenemase-producing CRE isolates were meropenem-vaborbactam susceptible.
- The most common infection type was bloodstream infection (n=1,477; 67.5%).
- Susceptibility of these isolates to levofloxacin and piperacillin-tazobactam was 99.6% and 98.5%, respectively.
- The most common infection type was bloodstream infection (n=1,477; 67.5%).
- Susceptibility of these isolates to meropenem-vaborbactam was 99.6%.
- Susceptibility of these isolates was 99.6% to meropenem-vaborbactam, 98.5% to meropenem-vaborbactam.

Conclusions

- Meropenem-vaborbactam was very active, with 99.6% susceptibility when tested against Enterobacterales isolates causing infections in patients in the United States.
- 1.2% of these isolates were CRE.
- KPC was the most common carbapenemase.
- 100% of KPC-producing isolates and all 3 of the carbapenemase-producing CRE isolates were meropenem-vaborbactam susceptible.
- These data suggest that meropenem-vaborbactam would be an effective treatment option for hematology/oncology or transplant patients with infections caused by Gram-negative pathogens, including CRE not producing extended-spectrum β-lactamase or OXA carbapenemases.

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References


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