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Activity of Meropenem-Vaborbactam Tested against *Burkholderia* Species Isolates

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Introduction

- *Burkholderia* species can cause chronic and often severe respiratory tract infections in persons with cystic fibrosis (CF).
  - Infection caused by *Burkholderia cepacia* complex (BCC) isolates has been associated with poor outcomes in persons with CF and limits transplant options for this population.
- The treatment of *Burkholderia* infections is complicated by low cell permeability to most antimicrobial agents, the presence of β-lactamases, and expression of efflux systems that can encode resistance to multiple classes.
- *Burkholderia* species are highly resistant to many antimicrobial agents and susceptibility results should only be reported for BCC against ceftazidime, meropenem, levofloxacin, minocycline, and trimethoprim-sulfamethoxazole.
- Recent studies demonstrated good activity of newer β-lactam/β-lactamase inhibitors against BCC isolates.
- We expanded this knowledge by evaluating the activity of meropenem-vaborbactam and comparator agents tested against *Burkholderia* spp. isolates collected during a global surveillance study.

Materials and Methods

- A total of 328 *Burkholderia* spp. isolates were received as part of a global surveillance program from 2014 to 2022.
  - Isolates were identified as the cause of infection per study protocol.
  - Isolates were limited to 1 per patient.
- Isolates were identified using the Bruker Biotyper MALDI-TOF MS according to the manufacturer instructions.
- Isolates were susceptibility tested against meropenem-vaborbactam and comparator agents using the reference broth microdilution method as described by the Clinical and Laboratory Standards Institute (CLSI) M07 (2018) and M100 (2023) documents.
  - Comparator agents included minocycline, ceftazidime, levofloxacin, and trimethoprim-sulfamethoxazole, as recommended by CLSI guidelines.
  - Vaborbactam was tested at a fixed concentration of 8 mg/L.
- Quality control (QC) was performed according to the CLSI M100 (2023) criteria.
  - All QC MIC results were within acceptable ranges.
- Categorical interpretations for BCC were those criteria found in the CLSI M100 (2023).
  - Meropenem breakpoints were applied for meropenem-vaborbactam for comparison purposes.

Results

- Among 328 *Burkholderia* spp. isolates received, 300 belonged to the BCC including 11 *B. cenocepacia* and 21 *B. multivorans* (Figure 1).
  - The remaining 28 isolates were *B. gladioli*, which is not a member of the BCC.
- Meropenem-vaborbactam ($MIC_{50/90}$, 1/2 mg/L) inhibited 95.3% of the BCC isolates at ≤4 mg/L and 97.0% at ≤8 mg/L (Figure 2A).
  - 96.4% and 100% of the *B. gladioli* isolates were inhibited by meropenem-vaborbactam ($MIC_{50/90}$, 0.5/2 mg/L) at ≤4 mg/L and ≤8 mg/L, respectively (Figure 2B).
  - Meropenem and meropenem-vaborbactam ($MIC_{50/90}$, 0.5/2 mg/L) exhibited the same activity against 28 *B. gladioli* isolates (Figure 2B).
  - Minocycline exhibited high susceptibilities against all *Burkholderia* groups (82.5% to 90.9%) at a breakpoint of 4 mg/L.
- The potency of meropenem-vaborbactam (MIC_{50}, 2 mg/L) was greater than the potency of all other agents tested against BCC isolates (MIC_{50} for all agents at ≥4 mg/L; Figure 2A).
- Trimethoprim-sulfamethoxazole, meropenem, and ceftazidime were active against 87.0%, 86.3%, and 84.6% of the BCC isolates, respectively.
  - Levofloxacin and minocycline inhibited 62.3% and 83% of BCC isolates, respectively.
- Trimethoprim-sulfamethoxazole, meropenem, meropenem-vaborbactam, and ceftazidime were active against all 11 *B. cenocepacia* isolates (100% susceptible; Figure 3).
  - Levofloxacin was active against only 54.5% of the *B. cenocepacia* isolates.
- Against a subset of 21 *B. multivorans* isolates, meropenem-vaborabactam ($MIC_{50/90}$, 0.5/2 mg/L) inhibited 95.2% of the isolates at ≤4 mg/L or ≤8 mg/L while meropenem inhibited 71.4% of the isolates at ≤4 mg/L and 95.2% of the isolates at ≤8 mg/L.
  - Trimethoprim-sulfamethoxazole and ceftazidime were active against 71.4% and 81.0% of the *B. multivorans* isolates.

Conclusions

- Meropenem-vaborbactam demonstrated the highest potency against BCC isolates that are commonly recovered from CF patients, including subsets of *B. multivorans* and *B. cenocepacia*.
  - This agent inhibited >90% of isolates belonging to BCC and subspecies when applying the meropenem CLSI breakpoint criterion.
- *B. cenocepacia* isolates seem more susceptible to most antimicrobial agents; however, *B. multivorans* isolates displayed higher resistance rates against trimethoprim-sulfamethoxazole, meropenem, and ceftazidime.
- The treatment options for BCC are limited and the use of meropenem-vaborbactam against infections caused by this organism group should be further investigated.

Figure 1. Species distribution among 328 *Burkholderia* spp. isolates

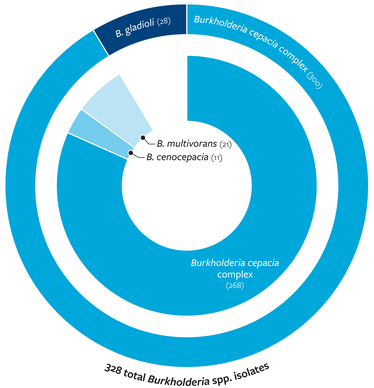


Figure 2. Finlandogram of the activity of antimicrobial agents tested against 328 *Burkholderia* spp. isolates

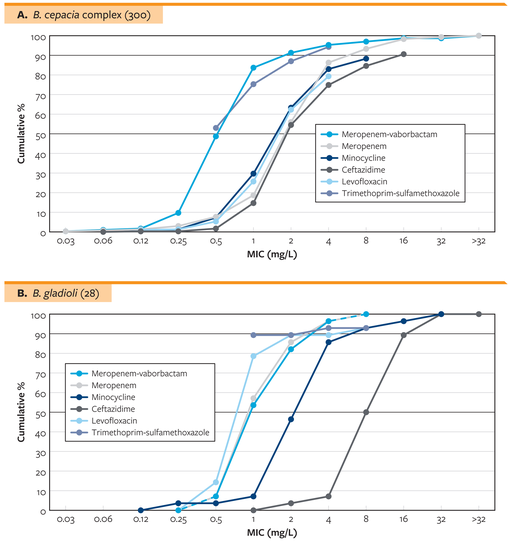
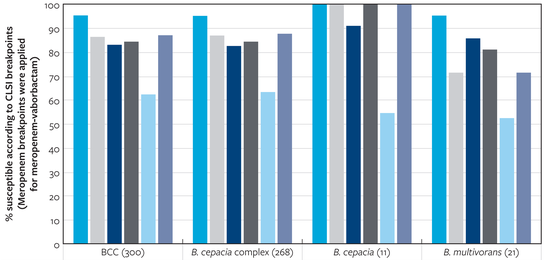


Figure 3. Activity of antimicrobial agents tested against 300 *Burkholderia cepacia* complex isolates



	BCC (300)	*B. cepacia* complex (268)	*B. cepacia* (11)	*B. multivorans* (21)
MER-VAB	95.3	95.1	100.0	95.2
MER	86.3	86.9	100.0	71.4
Mino	83.0	82.5	90.9	85.7
Ceftaz	84.3	84.3	100.0	81.0
Levo	62.3	63.3	54.5	52.4
T/S	87.0	87.6	100.0	71.4

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