

In Vitro Activity of Doripenem against *Burkholderia cepacia* Complex Isolates from Non-Cystic Fibrosis Patients[▽]

Burkholderia cepacia complex (BCC), a group of nonfermenting Gram-negative bacilli (NFGNB), is emerging as an important nosocomial pathogen. It causes a wide variety of infections, such as pneumonia (especially in patients with cystic fibrosis), meningitis, and septicemia. These infections are often difficult to treat due to high intrinsic antimicrobial resistance in BCC and the lack of effective antibiotics. BCC is resistant to aminoglycosides, antipseudomonal penicillins, and cephalosporins (4). Hence, the need for new agents active against this pathogen has become critical for patient care.

In recent years, carbapenems have assumed a greater therapeutic role for multidrug-resistant (MDR) isolates. Doripenem is a new broad-spectrum intravenous 1- β -methyl carbapenem. It has high activity against many Gram-positive and -negative organisms, including NFGNB. Against *Pseudomonas aeruginosa*, doripenem exhibits rapid bactericidal activity, with 2- to 4-fold-lower MICs than those of meropenem. However, the activity of doripenem against BCC has not been reported much, and present susceptibility reports are mainly from isolates of cystic fibrosis patients (6). Isolation of BCC from blood of non-CF septicemic patients is on the rise in our region (3), and the *in vitro* activity of doripenem against these isolates has been studied.

Fifty blood isolates of BCC obtained between May 2007 and January 2010 were included in this study. These isolates were identified using standard biochemical tests and confirmed using *recA* PCR-based restriction fragment length polymorphism (RFLP) analysis as described by Mahenthiralingam et al. to identify species (5). *B. cenocepacia* (genomovar IIIA) was the most prevalent species of BCC obtained. Pure cultures of the isolates were lyophilized and stored at 4°C. The meropenem susceptibilities of these 50

isolates were determined by the disk diffusion method (Astra Zeneca Pvt. Ltd., India) according to CLSI guidelines, with 8 isolates (16%) being meropenem resistant. *In vitro* susceptibility to doripenem (Ranbaxy Intensiva, India) was determined by the Etest. Etest strips (bioMérieux India Pvt. Ltd.) were used per the instructions of the manufacturer. In addition, *Escherichia coli* ATCC 25922 and *P. aeruginosa* ATCC 27853 were tested for quality control, and MICs obtained for these organisms were within the ranges recommended by the CLSI (2a). A distribution of the MICs of doripenem determined by the Etest for 50 strains of BCC is shown in Fig. 1.

The MIC values classifying isolates as susceptible or resistant to doripenem suggested by Bhavnani et al. (2) and Andes et al. (1) indicate susceptibility at ≤ 4 mg/liter and resistance at ≥ 16 mg/liter, with intermediate resistance being inferred as 8 mg/liter. Since there are no FDA- or CLSI-approved breakpoints at this time for doripenem, the MIC values obtained were interpreted based on the above criteria, with all 50 isolates (100%) of BCC being susceptible to doripenem (MIC ≤ 4 mg/liter). A greater proportion of strains among meropenem-resistant BCC were inhibited by doripenem at 2 mg/liter (Fig. 1).

Therefore, the *in vitro* susceptibility profile of BCC to doripenem is comparable to those of BCC to meropenem, and it can be an effective therapy for BCC strains resistant to meropenem.

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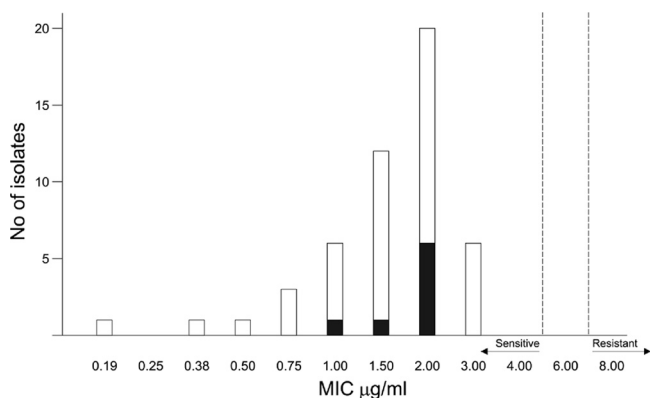


FIG. 1. Distribution of the MICs of doripenem determined by Etest for 50 strains of BCC. Black bars represent meropenem-resistant isolates.

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