NOTES

Carbapenem Susceptibility Patterns for Clinical Isolates of *Mycobacterium abscessus* Determined by the Etest Method[▽]

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***Mycobacterium abscessus* is resistant to multiple antibiotics, creating treatment challenges. Carbapenems are tested to increase therapeutic alternatives. We performed *in vitro* susceptibility testing by Etest of four carbapenems for *M. abscessus* isolates. Imipenem demonstrated the most *in vitro* activity, and testing of other carbapenems provided no additional value.**

Mycobacterium abscessus is a rapidly growing mycobacterium associated with pulmonary, skin, and soft-tissue infections, especially those that occur after cosmetic surgery, and is the third most frequently recovered nontuberculous mycobacterium (2, 4). Infection due to resistant *M. abscessus* is difficult to treat because it is resistant to multiple antibiotics, including imipenem (5). The latest Clinical and Laboratory Standards Institute (CLSI) guideline recommends testing and reporting susceptibility to amikacin, ceftiofloxacin, ciprofloxacin, clarithromycin, doxycycline, linezolid, and sulfamethoxazole (9).

To date, the most reliable and accurate method for susceptibility testing of rapidly growing *Mycobacterium* spp. has not been resolved, but the Etest (AB Biodisk, bioMérieux) method has shown promising results (1, 6, 8). In fact, the interlaboratory reproducibility of the Etest for the determination of the susceptibility of rapidly growing *Mycobacterium* spp. to imipenem has been reported to be 88 to 100% by interpretive category (1, 12). The objective of this study was to compare the *in vitro* activities of the newer carbapenems using the Etest method for clinical isolates identified as *M. abscessus*.

From October 2008 to February 2009, 108 clinical isolates identified as *M. abscessus* at ARUP Laboratories were collected consecutively and prospectively. Briefly, the identification of rapidly growing mycobacteria was performed by 16S rRNA sequencing by a standard laboratory protocol (11). Isolates identified as belonging to the *M. chelonae/abscessus* complex underwent an additional PCR assay using specific primers designed to distinguish *M. chelonae* from *M. abscessus* (3). No unique clusters of nucleotide sequences were identified. Each isolate was subcultured on sheep blood agar. A suspension was prepared in broth to a 1 McFarland standard and plated on

Mueller-Hinton agar with sheep blood. Etest strips were placed according to the manufacturer's instructions. The MICs of imipenem, meropenem, ertapenem, and doripenem were determined by the Etest method and read at day 3 of incubation. For each isolate, the MIC of imipenem and its susceptibility category were interpreted according to published guidelines: MIC of ≤ 4 $\mu\text{g/ml}$, susceptible; MIC of 8 $\mu\text{g/ml}$, intermediate; MIC of ≥ 16 $\mu\text{g/ml}$, resistant (9). Since there are currently no interpretive breakpoints available for meropenem, ertapenem, and doripenem, imipenem MIC breakpoints were applied.

For 108 isolates, 92 (85%) had no zones of inhibition with any carbapenem (Table 1). Overall, 103 (95%) isolates were interpreted as resistant to all carbapenems. Sixteen isolates had zones of inhibition (MICs of 2 to 32 $\mu\text{g/ml}$) with imipenem. Two isolates were interpreted as susceptible to imipenem (MICs of ≤ 4 $\mu\text{g/ml}$), and three were interpreted as intermediate (MICs of 8 $\mu\text{g/ml}$). Two isolates had zones of inhibition (MICs of 32 $\mu\text{g/ml}$) with meropenem, one had a zone of inhibition (MIC of 32 $\mu\text{g/ml}$) with ertapenem, and one had a zone of inhibition (MIC of 16 $\mu\text{g/ml}$) with doripenem. The zones of inhibition that were observed across all carbapenems were from the same isolate. When zones of inhibition were present, they were ill defined and elliptical for most of the isolates.

This is the first study to compare *in vitro* activities among carbapenems against *M. abscessus*. Although we did not perform broth microdilution, Etest previously has been shown to be an acceptable alternative to the broth microdilution method (1, 6, 8). Regardless of the test method, reporting imipenem is not recommended by CLSI guidelines because of concern for a lack of reliable, reproducible laboratory results. Rapidly growing *Mycobacterium* spp. are known to occasionally have inadequate growth for interpretation at 72 h, making determinations of carbapenem MICs difficult because of antibiotic degradation over time. For all 108 isolates in our study, growth was adequate for MIC determination at 72 h. We found that *M. abscessus* resistance to imipenem was very high at 95.4%, an observation not consistent with previous studies that found resistance to range between 55 and 88% (7, 10, 13). We hy-

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TABLE 1. MICs of carbapenems determined by Etest for 108 isolates

Zone (MIC, μ g/ml)	No. of isolates with MIC			
	Imipenem	Meropenem	Ertapenem	Doripenem
2	1	0	0	0
4	1	0	0	0
8	3	0	0	0
16	8	0	0	1
32	3	2	1	0
None	92	106	107	107

pothesize that the higher number of resistant isolates in our cohort may reflect the fact that ARUP Laboratories is a national reference laboratory and often multiple-drug-resistant organisms are referred to our laboratory for confirmatory testing.

In conclusion, carbapenems, including the more recently developed ones, have minimal activity against *M. abscessus*, with imipenem having the most *in vitro* activity. Certainly, we cannot draw conclusions about *in vivo* activity, clinical efficacy, or the role of combination carbapenem therapy. We acknowledge that clinicians may have limited treatment options for multiple-drug-resistant *M. abscessus* isolates, especially for patients with chronic kidney disease. However, our data demonstrate that when an isolate is resistant to imipenem, further testing of meropenem, ertapenem, and doripenem would provide no additional value. Hence, laboratories should deny such requests to prevent suspension of clinicians' investigations for other therapeutic alternatives while waiting for test results.

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