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Evaluation of the VITEK2 AST-N397 card and the ETEST for Antimicrobial Susceptibility Testing of *Enterobacterales* and *Pseudomonas aeruginosa* isolates

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INTRODUCTION

Escherichia coli, *Klebsiella pneumoniae* and *Pseudomanas aeruginosa* are the leading causes of healthcare-associated infections involving gram-negative bacteria. The rapid and global dissemination of multidrug-resistant organisms (MDROs) has become as a global public health concern leaving clinicians with few treatment options. New antibiotics based on the combination of a β-lactam with a new β-lactamase inhibitor, such as ceftazidime-avibactam and ceftolozane-tazobactam, have been developed with various efficacy against MDROs depending on the resistance mechanism. Consequently, implementation of effective treatment depends on the accuracy of antimicrobial susceptibility testing (AST) methods in the detection of resistance. Although broth microdilution (BMD) is the gold standard method to perform AST, most laboratories use several commercial automated AST systems for routine clinical testing. Among other methods, the easy-to-perform gradient diffusion method may also be used to obtain MIC values.

AIM

In this work we investigate the performances of the new VITEK2 AST-N397 card and ETEST gradient diffusion method (both from bioMérieux) for testing susceptibility to ceftazidime-avibactam (CAA), ceftolozane-tazobactam (CTA), meropenem (MEM), amikacin (AK) and gentamicin (GM) with a collection of *Enterobacterales* and *P.aeruginosa* isolates.

METHOD

Three hundred isolates (207 *Enterobacterales* and 93 *Pseudomonas aeruginosa*) were included for testing. One hundred and seventy-six isolates (58.7%) harboured at least one of the following carbapenemase genes: bla_{IMP}, bla_{KPC}, bla_{NDM}, bla_{OXA-48} or bla_{VIM}. For each isolate, a single initial McFarland suspension was prepared for inoculation of VITEK2 cards, ETEST strips, and BMD panels (MERLIN Diagnostica GmbH, Bornheim, Germany) for comparative testing. The 2021 EUCAST standards were used to interpret AST results. VITEK2 and ETEST results were compared with BMD results. Comparative performances were evaluated using essential agreement (EA), categorical agreement (CA), very major discrepancies [VMDs (false susceptibility)], major discrepancies [MDs (false resistance)] and minor discrepancies [mDs (intermediate result instead of susceptible or resistant)]. Essential agreement (EA) was defined as an MIC ±1 doubling dilution of the BMD MIC. Because of differences in the tested concentration range (Figure 1), the number of tests for evaluable EA calculation varied depending on each antimicrobial agent. Discrepancies (i. e., VMD or MD or mD) were resolved by a onetime triplicate testing. EA, CA, VMEs, MEs, and mEs were calculated after repeat testing.

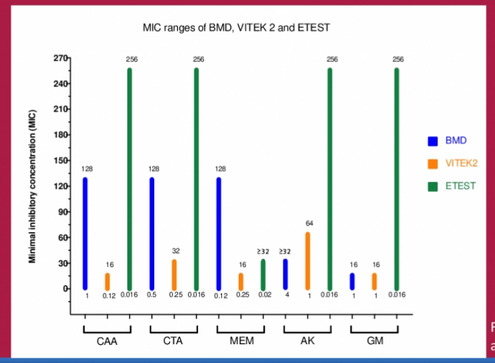

Figure 1: MIC ranges of BMD, VITEK2 and ETEST

RESULTS

Enterobacterales[a]	Method	S	I	R	TOT	EA (%)	CA (%)	MD (%)	VMD (%)	mD (%)
E. coli										
CAA	BMD	37	0	23	60					
	VITEK®2 N397card	37	0	23	60	1/1 (100)	60 (100)	0	0	0
	ETEST	37	0	23	60	4/6 (66.7)	60 (100)	0	0	0
CTA	BMD	26	0	34	60					
	VITEK®2 N397card	25	0	35	60	12/13 (92.3)	59 (98.3)	1 (3.8)	0	0
	ETEST	26	0	34	60	16/16 (100)	60 (100)	0	0	0
MEM	BMD	41	3	16	60					
	VITEK®2 N397card	35	2	23	60	3/15 (20.0)	51 (85.0)	6 (14.6)	0	3 (5.0)
	ETEST	40	4	16	60	29/32 (90.6)	59 (98.3)	0	0	1 (1.7)
AK	BMD	56	0	4	60					
	VITEK®2 N397card	55	0	5	60	3/3 (100)	59 (98.3)	1 (1.8)	0	0
	ETEST	55	0	5	60	3/3 (100)	59 (98.3)	1 (1.8)	0	0
GM	BMD	38	0	22	60					
	VITEK®2 N397card	38	0	22	60	53/53 (100)	60 (100)	0	0	0
	ETEST	38	0	22	60	5/5 (100)	60 (100)	0	0	0
K. pneumoniae										
CAA	BMD	85	0	39	124					
	VITEK®2 N397card	83	0	41	124	35/41 (85.4)	120 (96.8)	3 (3.5)	1 (2.6)	0
	ETEST	85	0	39	124	46/49 (93.9)	124 (100)	0	0	0
CTA	BMD	6	0	118	124					
	VITEK®2 N397card	5	0	119	124	4/8 (50.0)	123 (99.2)	1 (16.7)	0	0
	ETEST	6	0	118	124	55/58 (94.8)	124 (100)	0	0	0
MEM	BMD	25	8	91	124					
	VITEK®2 N397card	25	4	95	124	17/17 (100)	120 (96.8)	0	0	4 (3.2)
	ETEST	25	8	91	124	89/94 (94.7)	122 (98.4)	0	0	2 (1.6)
AK	BMD	70	0	54	124					
	VITEK®2 N397card	70	0	54	124	4/4 (100)	124 (100)	0	0	0
	ETEST	70	0	54	124	4/4 (100)	124 (100)	0	0	0
GM	BMD	54	0	70	124					
	VITEK®2 N397card	54	0	70	124	106/106 (100)	124 (100)	0	0	0
	ETEST	54	0	70	124	7/7 (100)	124 (100)	0	0	0
Others										
CAA	BMD	3	0	20	23					
	VITEK®2 N397card	3	0	20	23	1/1 (100)	23 (100)	0	0	0
	ETEST	3	0	20	23	4/5 (80.0)	23 (100)	0	0	0
CTA	BMD	1	0	22	23					
	VITEK®2 N397card	1	0	22	23	2/3 (66.7)	23 (100)	0	0	0
	ETEST	1	0	22	23	2/2 (100)	23 (100)	0	0	0
MEM	BMD	10	3	10	23					
	VITEK®2 N397card	10	0	13	23	5/7 (71.4)	20 (87.0)	0	0	3 (13.0)
	ETEST	11	2	10	23	2/2 (100)	22 (95.7)	0	0	1 (4.3)
AK	BMD	21	0	2	23					
	VITEK®2 N397card	21	0	2	23	-	23 (100)	0	0	0
	ETEST	21	0	2	23	-	23 (100)	0	0	0
GM	BMD	18	0	5	23					
	VITEK®2 N397card	18	0	5	23	17/17 (100)	23 (100)	0	0	0
	ETEST	18	0	5	23	6/7 (85.7)	23 (100)	0	0	0

TABLE 1. Overall performance of VITEK2-N397card and ETEST compared to BMD for 60 *Escherichia coli*, 124 *K.* pneumoniae and 23 Enterobacterales isolates other than *E. coli* and *K. pneumoniae*.

BMD results showed that 56% of the isolates were resistant to MEM, 70.3% to CTA, 46.9% to GM, 37.7% to CAA and 26.6% to AK. The evaluable EA between VITEK2 and BMD *Enterobacterales* and *P. aeruginosa* was 91.1% and 91.5%, respectively (Tables 1 and 2). The CA for *Enterobacterales* and *P. aeruginosa* was 97.8% and 99.7%, respectively. Among the *Enterobacterales* isolates, there was only one VMD for a *K. pneumoniae* bla_{NDM-1} isolate and CAA when tested with the VITEK-2 system. Three MDs for CAA and one for CTA were observed among *K. pneumoniae* isolates. One MD for CTA, one for AK and six for MEM were found among the *E.coli* isolates. There were eleven mDs for MEM, ten observed in *Enterobacterales* and one in *P. aeruginosa* isolates. No VMDs and MDs were found among *P. aeruginosa* isolates.

The evaluable EA between ETEST and BMD for *Enterobacterales* and *P. aeruginosa* was 92.9% and 96.5%, respectively. The CA for *Enterobacterales* and *P. aeruginosa* was 99.5% and 99.2%, respectively. One MD for AK and four mDs for MEM were observed among the *Enterobacterales* isolates. Among *P. aeruginosa* isolates, one MD for AK and 2 mDs for MEM were observed.

P. aeruginosa	Method	S	I	R	TOT	EA (%)	CA (%)	MD (%)	VMD (%)	mD (%)
CAA	BMD	62	0	31	93					
	VITEK®2 N397card	62	0	31	93	59/62 (95.2)	93 (100)	0	0	0
	ETEST	62	0	31	93	79/82 (96.3)	93 (100)	0	0	0
CTA	BMD	56	0	37	93					
	VITEK®2 N397card	56	0	37	93	36/40 (90.0)	93 (100)	0	0	0
	ETEST	56	0	37	93	45/49 (91.8)	93 (100)	0	0	0
MEM	BMD	30	12	51	93					
	VITEK®2 N397card	29	13	51	93	31/33 (93.9)	92 (98.9)	0	0	1 (1.1)
	ETEST	30	10	53	93	80/82 (97.6)	91 (97.8)	0	0	2 (2.2)
AK	BMD	73	0	20	93					
	VITEK®2 N397card	73	0	20	93	14/18 (77.8)	93 (100)	0	0	0
	ETEST	72	0	21	93	16/17 (94.1)	92 (98.9)	1 (1.4)	0	0

TABLE 2. Overall performance of AST-397 card and ETEST compared to BMD for 93 *P. aeruginosa* isolates.

CONCLUSIONS

Although further studies are needed to evaluate their overall performance, our experience with a large series of MDROs indicates that both the VITEK2-N397cards and the ETEST methods provide reliable AST results for testing CAA, CTA, MEM, AK and GM susceptibilities.