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ORIGINAL RESEARCH

New Option for Antibiotic Susceptibility Testing in Clinical Practice: Performance Evaluation of AutoMic-i600 Automatic System Based on Broth Microdilution Method

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Background: The emergence of multidrug-resistant bacteria limits antibiotic efficacy, making accurate antimicrobial susceptibility testing (AST) essential for clinical decisions. Broth microdilution (BMD) is the gold standard but is impractical for routine application. Current automated AST systems improve efficiency but face accuracy or operational challenges, highlighting the need for reliable and user-friendly solutions.

Objective: This study aims to evaluate the performance of a novel automated AST system (AutoMic-i600) based on the BMD method for AST of common clinical bacteria.

Methods: A total of 229 clinical isolates (150 Gram-negative and 79 Gram-positive) were prospectively collected from microbiology laboratory between June 2023 and August 2023. We reported the comparison of the AutoMic-i600 and Vitek 2 systems for routine antibiotics, and also validated the detection performance of AutoMic-i600 for novel antibiotics, based on the BMD method.

Results: The overall essential agreement (EA) and categorical agreement (CA) between AutoMic-i600 and BMD were 93.2% and 93.5% for Gram-negative bacteria and 98.5% and 97.8% for Gram-positive bacteria, respectively. The overall EA and CA between Vitek 2 and BMD were 92.6% and 93.5% for Gram-negative bacteria and 97.9% and 97.4% for Gram-positive bacteria. Importantly, for drug-resistant bacteria, AutoMic-i600 demonstrated a higher overall agreement than Vitek 2 (EA: 98.1% vs 94.8%, CA: 97.5% vs 92.0%), especially in Gram-negative bacteria (EA: 97.7% vs 93.5%, CA: 97.7% vs 89.3%). The VME rate for Gram-negative bacteria using AutoMic-i600 was significantly lower than that of Vitek 2 (1.0% vs 2.9%). Novel antibiotics detected by AutoMic-i600 exhibited EA and CA rates exceeding 90.0%.

Conclusion: Based on these findings, we recommend that the AutoMic-i600 system could be a new option for routine AST testing in a clinical setting. Particularly for drug-resistant bacteria and novel antibiotics, detection with AutoMic-i600 may be more reliable, which could further contribute to the prevention and treatment of drug-resistant bacteria.

Keywords: antibiotic susceptibility testing, drug-resistant bacteria, AutoMic-i600 system, automate

Introduction

The widespread rise of multidrug-resistant and extensively drug-resistant bacteria is increasingly limiting the effectiveness of current drugs and significantly causing treatment failure. Antimicrobial susceptibility testing (AST), as an essential tool, generally plays a highly influential role in guiding treatment.[1,2] Therefore, an accurate and reliable susceptibility test is crucial to directing clinical decisions.

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Broth microdilution (BMD) is the reference method that can detect the minimum inhibitory concentration (MIC) of antimicrobial drugs accurately and effectively.[3] But it is complex, costly, time-consuming, and not appropriate for daily testing in clinical laboratories. The Vitek 2 Compact system is widely used for commercial automated AST and employed in an overwhelming majority of hospitals in China.[4,5] However, there is still some controversy about the AST results of Vitek 2, especially regarding the detection of drug-resistant bacteria and potential false-sensitivity.[6–12] Similarly, the Phoenix automated system, another commonly used AST platform, has shown high concordance with reference methods for some antibiotics but exhibits reduced accuracy in determining the susceptibility of carbapenem-resistant Enterobacteriaceae (CRE) and methicillin-resistant *S. aureus* (MRSA) isolates.[13,14] And its operation is relatively cumbersome, requiring manual sample pipetting and information entry. In addition, the MicroScan WalkAway system includes a broad range of antibiotics, but the relatively long detection cycle (16–24 hours) may limit its applicability in urgent testing scenarios.[15] These findings underscore the importance of the accuracy and convenience in automated AST systems, enabling the rational selection of antimicrobial agents in clinical practice.

AutoMic-i600, a novel automatic microbial identification and susceptibility test system based on BMD, has been used in microbiology laboratories in recent years.[16] Clinical breakpoints are completely covered in the detectable range, and four-wavelength detection technology is employed to detect the turbidity and/or colour intensity of microdilution wells. The MIC values are actually detected rather than predicted, which may contribute to the accuracy of the test results. It also supports a fully automatic system of sample pipetting, incubation, and detection, exhibiting a high degree of automation.[17] Furthermore, the antibiotics on the single AST plate of AutoMic-i600 are more comprehensive and updated compared to Vitek 2, including the novel antibiotics, which are relatively newly incorporated into the automated AST system or approved and used in China recently with either under-reported or controversial performance, such as ceftazidime/avibactam, oritavancin, and cefoperazone/sulbactam. Currently, there is only one study demonstrating the accuracy of the AutoMic-i600 system in antifungal susceptibility testing.[18] Our study is the first to evaluate the performance of the AutoMic-i600 system in bacterial AST.

In this study, we compared the detection performance of the AutoMic-i600 system with that of the Vitek 2 system for routine antibiotics, based on the reference BMD method. And the novel antibiotics, which were newly approved in China and not available in the commonly used test cards of Vitek 2, were detected and comparatively analyzed by the AutoMic-i600 and BMD method. The aim is to assess the performance of the AutoMic-i600 system in detecting antimicrobial susceptibility for both routine and novel antibiotics, including its accuracy, validity, and potential benefits. This may provide a reliable new option for clinical AST, and support timely and effective treatment decisions in the face of increasingly serious antimicrobial resistance.

Materials and Methods

Study Design and Bacterial Isolates

A total of 75 strains of Enterobacteriaceae (33 Klebsiella pneumoniae, 27 Escherichia coli, 15 Enterobacter spp)., 75 strains of non-fermenting bacteria (31 Pseudomonas aeruginosa, 10 Acinetobacter baumannii, 15 Burkholderia cepacia, 19 Stenotrophomonas maltophilia), and 79 strains of Gram-positive cocci (33 Staphylococcus aureus, 15 Coagulase-negative staphylococci, 26 Enterococcus faecalis, 5 Enterococcus faecium) clinical isolates were collected between June 2023 and August 2023 from a tertiary A hospital in China. All isolated clinical strains were identified using a mass spectrometer, the Zybio EXS 2600 system (Zybio Inc., China). The principle and operation method are shown in Supplementary File 1. The specimen sources mainly included respiratory secretions, urine, blood, wounds, tissues, and fluids. Duplicate bacteria from the same patient and site had been excluded. Quality control was ensured by concurrent testing of four quality control strains, including E. coli ATCC 25922, P. aeruginosa ATCC 27853, S. aureus ATCC 29213, and E. faecalis ATCC 29212.

AST by the AutoMic-i600 System

The AST was performed using the AutoMic-i600 system (Autobio Diagnostics CO., Ltd., Zhengzhou, China) with strict adherence to the manufacturer's instructions (Supplementary File 2). Specifically, the measurement principles of the

AutoMic-i600 system are based on the broth microdilution method combined with the redox method for detecting MIC values. The AST Plate is coated with varying concentrations of antimicrobial agents at appropriate well locations. 100 µL of the bacterial suspension (0.5 McFarland) and one drop of the indicator solution (colorimetric oxidation-reduction) are added to 1 vial of broth and mixed well to prepare the inoculum suspension. Then, the suspension and the corresponding AST plate are placed in the instrument. A 100 µL suspension is automatically dispensed into each well, followed by automated incubation of the AST plate. After incubation, four-wavelength detection technology is employed to detect the MICs based on changes in the indicator as well as bacterial turbidity. And all MIC values are actually detected rather than predicted (Figure 1). The corresponding Enterobacteriaceae (EB), non-fermenters (NF) and Gram-positive (GP) AST plates were used for Enterobacteriaceae, non-fermenting bacteria, and Gram-positive cocci, respectively.

AST by the Vitek 2 System and the BMD Method

We performed AST with the Vitek 2 system (bioMérieux, Marcy l'Etoile, France) according to the manufacturer's instructions, using the software version 8.01 and the AST-GN13, AST-N335, and AST-GP67 cards for Enterobacteriaceae, non-fermenting bacteria, and Gram-positive cocci, respectively. The Vitek 2 system employs a solely turbidimetric method (three-wavelength), measuring bacterial growth by detecting 3–4 concentrations of antibiotics and inferring the MICs based on growth kinetics. We performed AST by the BMD method according to the Clinical and Laboratory Standards Institute (CLSI) M100-Ed33 guideline.[19]

Discrepancy Resolution and Data Analysis

The AutoMic-i600 system and Vitek 2 system AST results were compared with the BMD results. For most antibiotics, the clinical breakpoints were interpreted according to the CLSI M100-Ed33 standards.[19] Since CLSI does not provide interpretive criteria for cefoperazone/sulbactam, we adopted the criteria reported in previous studies, which defined the breakpoints as susceptibility (≤16 mg/L), intermediate (32 mg/L), and resistance (≥64 mg/L).[20] Moxifloxacin breakpoints for Enterobacteriaceae and colistin breakpoints for non-fermenting bacteria were referenced in European Committee on Antimicrobial Susceptibility Testing (EUCAST) standards.[21] And tigecycline breakpoints were interpreted following the Food and Drug Administration (FDA) standards.[22] The breakpoint criteria used by AutoMic-i600 are the same as those of Vitek 2 (Supplementary File 3). Essential agreement (EA) and bias were calculated according to the recommendations in the ISO 20776–2:2021 document.[23] Congruent expected performances were as follows: EA≥90%, −30%≤bias ≤

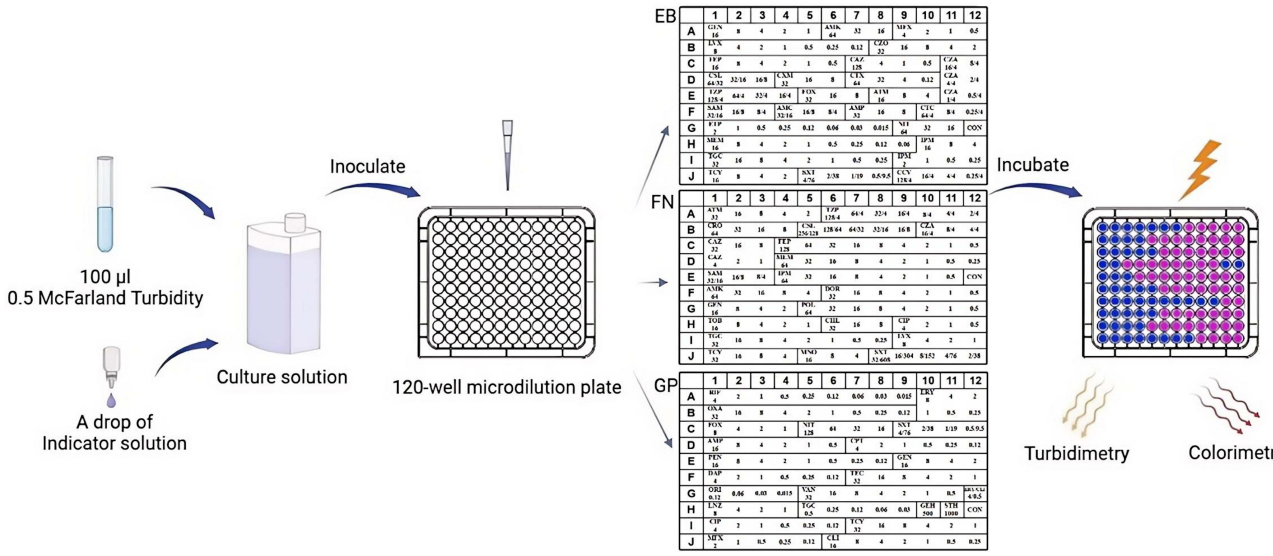

Figure 1 The detection method and principle of the AutoMic-i600 system. Clinical breakpoints were completely covered in the 120-well microdilution plate. Colorimetric and turbidimetric methods (four-wavelength) were combined to measured MIC values. Fully automated sample pipetting, incubation, detection and continuous interpretation (every 30 minutes regularly) were supported.

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+30%. Rates of categorical agreement (CA), very major errors (VMEs, false susceptibility), major errors (MEs, false resistance) and minor errors (mEs, intermediate result instead of susceptible or resistant) were also calculated following the definitions from ISO 20776–2:2007.[24,25] Expected congruent performances were: CA ≥ 90%, VMEs and MEs rates < 3%, and mE rates < 10%.

Results

Comparison of AST for Common Clinical Isolates

We included a total of 229 isolates (150 Gram-negative and 79 Gram-positive) isolated from clinical specimens, and performed tests against various antibiotics. For Gram-negative bacteria, 33 isolates of *K. pneumoniae* were tested against 13 antibiotics, 27 isolates of *E. coli* against 14 antibiotics, and other species against 4–11 antibiotics, resulting in 1544 organism/antimicrobial tests (Table 1). For Gram-positive bacteria, 48 isolates of staphylococci were tested against 15 antibiotics each, and 31 isolates of enterococci against 10 antibiotics each, totaling 1030 organism/antimicrobial tests (Table 2). All tests were performed using the AutoMic-i600 and Vitek 2 systems, with BMD as the reference method.

Among Gram-negative bacteria, the AutoMic-i600 system exhibited 93.2% EA (1439/1544) with a bias of 1.6%, and the Vitek 2 system exhibited 92.6% EA (1430/1544) with a bias of −12.7%. The CA was 93.5% for both AutoMic-i600 (1443/1544) and Vitek 2 (1444/1544) systems (Table 1). In Gram-positive bacteria, the AutoMic-i600 system exhibited 98.5% EA (859/872) with a bias of 1.2%, and the Vitek 2 system exhibited 97.9% EA (854/872) with a bias of −5.3%. The CA was 97.8% (1007/1030) for the AutoMic-i600 system and 97.4% (1003/1030) for the Vitek 2 system (Table 2). The overall rates of VMEs, MEs and mEs were 1.1% (7/612), 1.7% (31/1840) and 3.3% (86/2574) with the AutoMic-i600, and 2.3% (14/612), 0.7% (13/1840) and 3.9% (100/2574) with the Vitek 2 (Tables 1 and 2).

As depicted in Tables 1 and 2, we analyzed the distributions of agreements and errors for each antimicrobial agent concerning Gram-negative and Gram-positive bacteria, respectively. We noted that amikacin showed complete agreement (EA and CA both of 100%) in the two systems for Enterobacteriaceae (n = 75), as well as penicillin for Gram-positive cocci (n = 79). In gram-negative bacteria, both systems yielded high rates of mEs for levofloxacin and nitrofurantoin. Apart from mEs, most errors of the AutoMic-i600 were caused by MEs (2.4%), mainly observed in the detection of ceftazidime (*K. pneumoniae*, 13.3%; *E. coli*, 13.0%), cefepime (*E. coli*, 9.5%), and aztreonam (*P. aeruginosa*, 11.8%). While as for Vitek 2, the majority of error rates, except mEs, were attributed to a high rate of VMEs (2.9%), mainly observed for polymyxin (*P. aeruginosa*, 66.7%), cefepime (*K. pneumoniae*, 20.0%; *E. coli*, 20.0%), aztreonam (*K. pneumoniae*, 16.7%), minocycline (*B. cepacia*, 16.7%), and ceftazidime (*S. maltophilia*, 16.7%) (Table 1). Among gram-positive bacteria, the inducible clindamycin resistance-related VMEs were predominantly observed when using Vitek 2 (Table 2).

Agreement of AST in Drug-Resistant Bacteria

This study included 166 isolates resistant to one or more antimicrobials. Overall, the AutoMic-i600 AST results demonstrated 98.1% (529/539) essential and 97.5% (597/612) categorical agreement, and the Vitek 2 AST results demonstrated 94.8% (511/539) essential and 92.0% (563/612) categorical agreement (Table 3). When the performance of each system was stratified by type of drug-resistant bacteria, the EA rates of the AutoMic-i600 and Vitek 2 systems were 97.7% (301/308) and 93.5% (288/308) for Gram-negative bacteria, and 98.7% (228/231) and 96.5% (223/231) for Gram-positive bacteria, respectively. And CA rates of the AutoMic-i600 and Vitek 2 systems were 97.7% (301/308) and 89.3% (275/308) for Gram-negative bacteria, and 97.4% (296/304) and 94.7% (288/304) for Gram-positive bacteria, respectively.

Consistency Analysis of AST for Novel Antibiotics

We categorized the antibiotics, which are relatively newly incorporated into the automated AST system or approved and used in China in recent years with either under-reported or controversial performance as novel antibiotics. Using BMD as the reference method, we employed AutoMic-i600 to detect the sensitivity of *K. pneumoniae* (n = 33) and *E. coli* (n = 27)

Table 1 Performance of the AutoMic-i600 and the Vitek 2 Systems Compared With BMD for Gram-Negative Bacterial Species (n = 150)

Antimicrobial	BMD			AutoMic-i600 System (%)						Vitek 2 System (%)					
	S	I	R	Agreement		Errors			Bias	Agreement		Errors			Bias
				EA	CA	VMEs	MEs	mEs		EA	CA	VMEs	MEs	mEs	
K. pneumoniae (n = 33)															
Ceftazidime	30	0	3	87.9(29/33)	87.9(29/33)	0.0(0/3)	13.3(4/30)	0.0(0/33)	16.7	100.0(33/33)	100.0(33/33)	0.0(0/3)	0.0(0/30)	0.0(0/33)	−28.6
Cefepime	27	1	5	93.9(31/33)	93.9(31/33)	0.0(0/5)	0.0(0/27)	6.1(2/33)	−9.8	93.9(31/33)	93.9(31/33)	20.0(1/5)	0.0(0/27)	3.0(1/33)	−23.0
Aztreonam	26	1	6	100.0(33/33)	97.0(32/33)	0.0(0/6)	0.0(0/26)	3.0(1/33)	−4.3	93.9(31/33)	90.9(30/33)	16.7(1/6)	0.0(0/26)	6.1(2/33)	−26.7
Amikacin	32	0	1	100.0(33/33)	100.0(33/33)	0.0(0/1)	0.0(0/32)	0.0(0/33)	0.0	100.0(33/33)	100.0(33/33)	0.0(0/1)	0.0(0/32)	0.0(0/33)	0.0
Levofloxacin	22	4	7	93.9(31/33)	97.0(32/33)	0.0(0/7)	4.5(1/22)	0.0(0/33)	11.5	90.9(30/33)	90.9(30/33)	0.0(0/7)	0.0(0/22)	9.1(3/33)	−12.8
Imipenem	31	0	2	97.0(32/33)	97.0(32/33)	0.0(0/2)	3.2(1/31)	0.0(0/33)	3.1	100.0(33/33)	100.0(33/33)	0.0(0/2)	0.0(0/31)	0.0(0/33)	3.1
Ertapenem	30	1	2	97.0(32/33)	97.0(32/33)	0.0(0/2)	3.3(1/30)	0.0(0/33)	3.2	100.0(33/33)	97.0(32/33)	0.0(0/2)	0.0(0/30)	3.0(1/33)	−27.1
Nitrofurantoin	10	12	11	97.0(32/33)	87.9(29/33)	0.0(0/11)	0.0(0/10)	12.1(4/33)	7.1	93.9(31/33)	84.8(28/33)	0.0(0/11)	0.0(0/10)	15.2(5/33)	−17.9
Others[a]	122	8	35	96.4(159/165)	95.2(157/165)	0.0(0/35)	2.5(3/122)	3.0(5/165)	3.5	96.4(159/165)	95.2(157/165)	2.9(1/35)	0.0(0/122)	4.2(7/165)	−14.2
E. coli (n=27)															
Ceftazidime	23	0	4	85.2(23/27)	88.9(24/27)	0.0(0/4)	13.0(3/23)	0.0(0/27)	20.8	92.6(25/27)	100.0(27/27)	0.0(0/4)	0.0(0/23)	0.0(0/27)	−25.0
Cefepime	21	1	5	85.2(23/27)	85.2(23/27)	0.0(0/5)	9.5(2/21)	7.4(2/27)	17.3	85.2(23/27)	85.2(23/27)	20.0(1/5)	0.0(0/21)	11.1(3/27)	−35.8
Aztreonam	19	1	7	92.6(25/27)	85.2(23/27)	14.3(1/7)	5.2(1/19)	7.4(2/27)	3.5	88.9(24/27)	92.6(25/27)	0.0(0/7)	5.2(1/19)	3.7(1/27)	−9.0
Amikacin	27	0	0	100.0(27/27)	100.0(27/27)	NA(0/0)	0.0(0/27)	0.0(0/27)	0.0	100.0(27/27)	100.0(27/27)	NA(0/0)	0.0(0/27)	0.0(0/27)	0.0
Levofloxacin	6	5	16	92.6(25/27)	81.5(22/27)	6.7(1/16)	0.0(0/6)	14.8(4/27)	0.0	92.6(25/27)	81.5(23/27)	0.0(0/16)	0.0(0/6)	14.8(4/27)	8.0
Imipenem	27	0	0	100.0(27/27)	100.0(27/27)	NA(0/0)	0.0(0/27)	0.0(0/27)	3.7	100.0(27/27)	100.0(27/27)	NA(0/0)	0.0(0/27)	0.0(0/27)	0.0
Ertapenem	27	0	0	96.3(26/27)	96.3(26/27)	NA(0/0)	0.0(0/27)	3.7(1/27)	3.7	100.0(27/27)	100.0(27/27)	NA(0/0)	0.0(0/27)	0.0(0/27)	0.0
Nitrofurantoin	27	0	0	100.0(27/27)	100.0(27/27)	NA(0/0)	0.0(0/27)	0.0(0/27)	0.0	100.0(27/27)	100.0(27/27)	NA(0/0)	0.0(0/27)	0.0(0/27)	0.0
Others[b]	82	11	69	96.9(157/162)	97.5(158/162)	0.0(0/69)	0.0(0/82)	2.5(4/162)	4.0	96.3(156/162)	96.9(157/162)	0.0(0/69)	0.0(0/82)	3.1(5/162)	−13.7
Enterobacter spp. (n=15)															
Ceftazidime	13	0	2	93.3(14/15)	100.0(15/15)	0.0(0/2)	0.0(0/13)	0.0(0/15)	−4.0	100.0(15/15)	100.0(15/15)	0.0(0/2)	0.0(0/13)	0.0(0/15)	−25.0
Cefepime	14	0	1	93.3(14/15)	100.0(15/15)	0.0(0/1)	0.0(0/14)	0.0(0/15)	−13.3	100.0(15/15)	100.0(15/15)	0.0(0/1)	0.0(0/14)	0.0(0/15)	6.7
Aztreonam	11	1	3	86.7(13/15)	80.0(12/15)	0.0(0/3)	9.1(1/11)	13.3(2/15)	−8.3	93.3(14/15)	93.3(14/15)	0.0(0/3)	0.0(0/11)	6.7(1/15)	−25.0
Amikacin	15	0	0	100.0(15/15)	100.0(15/15)	NA(0/0)	0.0(0/15)	0.0(0/15)	0.0	100.0(15/15)	100.0(15/15)	NA(0/0)	0.0(0/15)	0.0(0/15)	0.0
Levofloxacin	13	1	1	93.3(14/15)	100.0(15/15)	0.0(0/1)	0.0(0/13)	0.0(0/15)	−25.0	100.0(15/15)	100.0(15/15)	0.0(0/1)	0.0(0/13)	0.0(0/15)	−26.2
Imipenem	14	1	0	93.3(14/15)	86.7(13/15)	NA(0/0)	7.1(1/14)	6.7(1/15)	−8.9	100.0(15/15)	93.3(14/15)	NA(0/0)	0.0(0/14)	6.7(1/15)	6.7
Ertapenem	14	1	0	93.3(14/15)	93.3(14/15)	NA(0/0)	7.1(1/14)	0.0(0/15)	13.3	93.3(14/15)	93.3(14/15)	NA(0/0)	0.0(0/14)	6.7(1/15)	6.7
Nitrofurantoin	5	4	6	93.3(14/15)	86.7(13/15)	0.0(0/6)	20.0(1/5)	6.7(1/15)	22.2	93.3(14/15)	86.7(13/15)	0.0(0/6)	0.0(0/5)	13.3(2/15)	−6.2
Others[c]	39	2	4	100.0(45/45)	100.0(45/45)	0.0(0/4)	0.0(0/39)	0.0(0/45)	0.0	95.6(43/45)	97.8(44/45)	0.0(0/4)	0.0(0/39)	2.2(1/45)	−14.3
P. aeruginosa (n=31)															
Ceftazidime	23	1	7	96.8(30/31)	93.5(29/31)	0.0(0/7)	0.0(0/23)	6.5(2/31)	8.4	96.8(30/31)	93.5(29/31)	0.0(0/7)	0.0(0/23)	6.5(2/31)	16.4
Cefepime	23	2	6	87.1(27/31)	83.9(26/31)	0.0(0/6)	4.3(1/23)	12.9(4/31)	18.7	90.3(28/31)	87.1(27/31)	0.0(0/6)	0.0(0/23)	12.9(4/31)	−9.8
Aztreonam	17	6	8	87.1(27/31)	80.6(25/31)	0.0(0/8)	11.8(2/17)	12.9(4/31)	23.0	87.1(27/31)	87.1(27/31)	0.0(0/8)	5.9(1/17)	9.7(3/31)	−18.9
Levofloxacin	19	4	8	96.8(30/31)	87.1(27/31)	0.0(0/8)	0.0(0/19)	12.9(4/31)	9.5	87.1(27/31)	87.1(27/31)	0.0(0/8)	0.0(0/19)	12.9(4/31)	−22.9
Colistin	28	0	3	96.8(30/31)	96.8(30/31)	0.0(0/3)	3.6(1/28)	0.0(0/31)	4.5	90.3(28/31)	93.5(29/31)	66.7(2/3)	0.0(0/28)	0.0(0/31)	−30.8
Imipenem	15	2	14	90.3(28/31)	93.5(29/31)	0.0(0/14)	0.0(0/15)	6.5(2/31)	19.5	96.8(30/31)	90.3(28/31)	0.0(0/14)	0.0(0/15)	9.7(3/31)	−7.8
Meropenem	18	1	12	90.3(28/31)	93.5(29/31)	8.3(1/12)	0.0(0/18)	3.2(1/31)	10.7	87.1(27/31)	83.9(26/31)	0.0(0/12)	5.6(1/18)	12.9(4/31)	15.8
Others[d]	99	7	18	93.5(116/124)	91.1(113/124)	0.0(0/18)	1.0(1/99)	8.1(10/124)	−11.2	91.9(114/124)	89.5%(111/124)	5.6(1/18)	3.0(3/99)	7.3(9/124)	1.7

(*Continued*)

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Table 1 (Continued).

Antimicrobial	BMD			AutoMic-i600 System (%)						Vitek 2 System (%)					
	S	I	R	Agreement		Errors			Bias	Agreement		Errors			Bias
				EA	CA	VMEs	MEs	mEs		EA	CA	VMEs	MEs	mEs	
A. baumannii (n=10)															
Ceftazidime	6	0	4	100.0(10/10)	100.0(10/10)	0.0(0/4)	0.0(0/6)	0.0(0/10)	14.3	100.0(10/10)	100.0(10/10)	0.0(0/4)	0.0(0/6)	0.0(0/10)	−1.4
Cefepime	4	2	4	90.0(9/10)	80.0(8/10)	0.0(0/4)	25.0(1/4)	10.0(1/10)	23.3	80.0(8/10)	80.0(8/10)	0.0(0/4)	0.0(0/4)	20.0(2/10)	−3.3
Levofloxacin	8	0	2	90.0(9/10)	90.0(9/10)	0.0(0/2)	0.0(0/8)	10.0(1/10)	0.0	100.0(10/10)	100.0(10/10)	0.0(0/2)	0.0(0/8)	0.0(0/10)	0.0
Imipenem	5	0	5	100.0(10/10)	100.0(10/10)	0.0(0/5)	0.0(0/5)	0.0(0/10)	3.3	90.0(9/10)	90.0(9/10)	0.0(0/5)	0.0(0/5)	10.0(1/10)	−8.6
SXT	9	0	1	100.0(10/10)	100.0(10/10)	0.0(0/1)	0.0(0/9)	0.0(0/10)	0.0	90.0(9/10)	90.0(9/10)	0.0(0/1)	11.1(1/9)	0.0(0/10)	10.0
Others[e]	21	3	6	96.7(29/30)	93.3(28/30)	0.0(0/6)	0.0(0/21)	6.7(2/30)	1.3	90.0(27/30)	86.7%(26/30)	0.0(0/6)	4.8(1/21)	10(3/30)	3.3
B. cepacia (n=15)															
Ceftazidime	13	1	1	93.3(14/15)	86.7(13/15)	0.0(0/1)	0.0(0/13)	13.3(2/15)	21.4	93.3(14/15)	93.3(14/15)	0.0(0/1)	0.0(0/13)	6.7(1/15)	−14.3
Minocycline	7	2	6	93.3(14/15)	86.7(13/15)	0.0(0/6)	0.0(0/7)	13.3(2/15)	5.7	93.3(14/15)	80.0(12/15)	16.7(1/6)	0.0(0/7)	13.3(2/15)	−22.2
Levofloxacin	11	2	2	93.3(14/15)	86.7(13/15)	0.0(0/2)	9.1(1/11)	6.7(1/15)	−13.3	81.8(9/15)	80.0(12/15)	0.0(0/2)	18.2(2/11)	6.7(1/15)	44.6
SXT	15	0	0	100.0(15/15)	100.0(15/15)	NA(0/0)	0.0(0/15)	0.0(0/15)	0.0	100.0(15/15)	100.0(15/15)	NA(0/0)	0.0(0/15)	0.0(0/15)	0.0
Meropenem	11	0	4	100.0(15/15)	100.0(15/15)	0.0(0/4)	0.0(0/11)	0.0(0/15)	−3.2	93.3(14/15)	93.3(14/15)	0.0(0/4)	0.0(0/11)	6.7(1/15)	−12.3
S. maltophilia (n=19)															
Ceftazidime	12	1	6	94.7(18/19)	94.7(18/19)	0.0(0/6)	0.0(0/12)	5.3(1/19)	9.7	94.4(18/19)	89.5(17/19)	16.7(1/6)	0.0(0/12)	5.3(1/19)	−12.0
Minocycline	19	0	0	100.0(19/19)	94.7(18/19)	NA(0/0)	0.0(0/19)	5.3(1/19)	5.3	100.0(19/19)	100.0(19/19)	NA(0/0)	0.0(0/19)	0.0(0/19)	0.0
Levofloxacin	17	1	1	89.5 (17/19)	84.2(16/19)	0.0(0/1)	0.0(0/17)	15.8(3/19)	11.6	89.5(17/19)	89.5(17/19)	0.0(0/1)	0.0(0/17)	10.5(2/19)	−17.5
SXT	19	0	0	94.7(18/19)	94.7(18/19)	NA(0/0)	0.0(0/19)	5.3(1/19)	5.3	100.0(19/19)	100.0(19/19)	NA(0/0)	0.0(0/19)	0.0(0/19)	0.0
Total (n = 150)	1146	90	308	93.2(1439/1544)	93.5(1443/1544)	1.0(3/308)	2.4(27/1146)	4.6(71/1544)	1.6	92.6(1430/1544)	93.5(1444/1544)	2.9(9/308)	0.9(10/1146)	5.2(81/1544)	−12.7

Notes: [a] Others included TZP, SAM, cefazolin, gentamicin and SXT; [b] Others included TZP, SAM, ampicillin, cefazolin, gentamicin and SXT; [c] Others included TZP, gentamicin and SXT; [d] Others included TZP, CSL, amikacin and tobramycin; [e] Others included TZP, CSL, and amikacin.

Abbreviations: NA, not applicable; S, susceptible; I, intermediate; R, resistant; TZP, piperacillin/tazobactam; SAM, ampicillin/Sulbactam; SXT, trimethoprim/Sulfamethoxazole; CSL, cefoperazone/sulbactam.

Table 2 Performance of the AutoMic-i600 and the Vitek 2 Systems Compared With BMD for Gram-Positive Bacterial Species (n = 79)

Antimicrobial	BMD			AutoMic-i600 system (%)						Vitek 2 system (%)					
	S	I	R	Agreement		Errors			Bias	Agreement		Errors			Bias
				EA	CA	VMEs	MEs	mEs		EA	CA	VMEs	MEs	mEs	
S. aureus (n = 33)															
Penicillin	6	0	27	100.0(33/33)	100.0(33/33)	0.0(0/27)	0.0(0/6)	0.0(0/33)	−3.7	100.0(33/33)	100.0(33/33)	0.0(0/27)	0.0(0/6)	0.0(0/33)	−3.6
Oxacillin	23	0	10	100.0(33/33)	100.0(33/33)	0.0(0/10)	0.0(0/23)	0.0(0/33)	23.6	97.0(32/33)	100.0(33/33)	0.0(0/10)	0.0(0/23)	0.0(0/33)	−19.7
Cefoxitin	21	0	12	NA	100.0(33/33)	0.0(0/12)	0.0(0/21)	0.0(0/33)	NA	NA	100.0(33/33)	0.0(0/12)	0.0(0/21)	0.0(0/33)	NA
Tetracycline	29	0	4	97.0(32/33)	97.0(32/33)	0.0(0/4)	0.0(0/29)	3.0(1/33)	6.3	100.0(33/33)	100.0(33/33)	0.0(0/4)	0.0(0/29)	0.0(0/33)	−16.6
Tigecycline	33	0	0	100.0(33/33)	100.0(33/33)	NA(0/0)	0.0(0/33)	0.0(0/33)	6.1	100.0(33/33)	100.0(33/33)	NA(0/0)	0.0(0/33)	0.0(0/33)	6.1
Gentamicin	32	1	0	97.0(32/33)	97.0(32/33)	NA(0/0)	0.0(0/32)	3.0(1/33)	3.0	97.0(32/33)	97.0(32/33)	NA(0/0)	0.0(0/32)	3.0(1/33)	−17.0
erythromycin	17	0	16	100.0(33/33)	100.0(33/33)	0.0(0/16)	0.0(0/17)	0.0(0/33)	17.6	100.0(33/33)	100.0(33/33)	0.0(0/16)	0.0(0/17)	0.0(0/33)	−10.0
Ciprofloxacin	26	0	7	100.0(33/33)	100.0(33/33)	0.0(0/7)	0.0(0/26)	0.0(0/33)	−6.1	97.0(32/33)	93.9(31/33)	0.0(0/7)	3.8(1/26)	3.0(1/33)	7.7
Moxifloxacin	26	2	5	97.0(32/33)	93.9(31/33)	0.0(0/5)	0.0(0/26)	6.1(2/33)	12.9	97.0(32/33)	93.9(31/33)	0.0(0/5)	0.0(0/26)	6.1(2/33)	−22.3
SXT	30	0	3	100.0(33/33)	100.0(33/33)	0.0(0/3)	0.0(0/30)	0.0(0/33)	6.5	100.0(33/33)	100.0(33/33)	0.0(0/3)	0.0(0/30)	0.0(0/33)	0.0
Clindamycin	26	1	6	100.0(33/33)	100.0(33/33)	0.0(0/6)	0.0(0/26)	0.0(0/33)	3.7	97.0(32/33)	97.0(32/33)	0.0(0/6)	0.0(0/26)	3.0(1/33)	−14.3
ICR	17	0	16	NA	100.0(33/33)	0.0(0/16)	0.0(0/17)	0.0(0/33)	NA	NA	90.9(30/33)	18.8(3/16)	0.0(0/17)	0.0(0/33)	NA
Linezolid	33	0	0	100.0(33/33)	100.0(33/33)	NA(0/0)	0.0(0/33)	0.0(0/33)	9.1	100.0(33/33)	100.0(33/33)	NA(0/0)	0.0(0/33)	0.0(0/33)	−3.0
Rifampin	33	0	0	100.0(33/33)	100.0(33/33)	NA(0/0)	0.0(0/33)	0.0(0/33)	0.0	100.0(33/33)	100.0(33/33)	NA(0/0)	0.0(0/33)	0.0(0/33)	0.0
Nitrofurantoin	33	0	0	100.0(33/33)	100.0(33/33)	NA(0/0)	0.0(0/33)	0.0(0/33)	0.0	100.0(33/33)	100.0(33/33)	NA(0/0)	0.0(0/33)	0.0(0/33)	3.0
CoNS (n = 15)															
Penicillin	0	0	15	100.0(15/15)	100.0(15/15)	0.0(0/15)	NA(0/0)	0.0(0/15)	0.0	100.0(15/15)	100.0(15/15)	0.0(0/15)	NA(0/0)	0.0(0/15)	0.0
Oxacillin	2	0	13	93.3(14/15)	93.3(14/15)	7.7(1/13)	0.0(0/2)	0.0(0/15)	−2.9	93.3(14/15)	100.0(15/15)	0.0(0/13)	0.0(0/2)	0.0(0/15)	20.9
Cefoxitin	2	0	13	NA	100.0(15/15)	0.0(0/13)	0.0(0/2)	0.0(0/15)	NA	NA	100.0(15/15)	0.0(0/13)	0.0(0/2)	0.0(0/15)	NA
Tetracycline	11	0	4	100.0(15/15)	100.0(15/15)	0.0(0/4)	0.0(0/11)	0.0(0/15)	0.0	100.0(15/15)	100.0(15/15)	0.0(0/4)	0.0(0/11)	0.0(0/15)	9.1
Tigecycline	15	0	0	93.3(14/15)	100.0(15/15)	NA(0/0)	0.0(0/15)	0.0(0/15)	−1.0	100.0(15/15)	100.0(15/15)	NA(0/0)	0.0(0/15)	0.0(0/15)	−18.3
Gentamicin	6	3	6	86.7(13/15)	80.0(12/15)	0.0(0/6)	0.0(0/6)	20.0(3/15)	18.9	93.3(14/15)	86.7(13/15)	0.0(0/6)	0.0(0/6)	13.3(2/15)	−22.2
Erythromycin	2	0	13	100.0(15/15)	100.0(15/15)	0.0(0/13)	0.0(0/2)	0.0(0/15)	0.0	100.0(15/15)	100.0(15/15)	0.0(0/13)	0.0(0/2)	0.0(0/15)	0.0
Ciprofloxacin	2	0	13	100.0(15/15)	100.0(15/15)	0.0(0/13)	0.0(0/2)	0.0(0/15)	−7.1	100.0(15/15)	100.0(15/15)	0.0(0/13)	0.0(0/2)	0.0(0/15)	0.0
Moxifloxacin	2	3	10	100.0(15/15)	93.3(14/15)	0.0(0/10)	0.0(0/2)	6.7(1/15)	13.2	86.7(13/15)	86.7(13/15)	0.0(0/10)	0.0(0/2)	13.3(2/15)	−23.1
SXT	10	0	5	93.3(14/15)	93.3(14/15)	20.0(1/5)	0.0(0/10)	0.0(0/15)	−23.3	86.7(13/15)	93.3(14/15)	0.0(0/5)	10.0(1/10)	0.0(0/15)	4.8
Clindamycin	12	0	3	93.3(14/15)	93.3(14/15)	0.0(0/3)	8.3(1/12)	0.0(0/15)	7.7	93.3(14/15)	93.3(14/15)	0.0(0/3)	0.0(0/12)	6.7(1/15)	−25.0
ICR	5	0	10	NA	93.3(14/15)	10.0(1/10)	0.0(0/5)	0.0(0/15)	NA	NA	86.7(13/15)	20.0(2/10)	0.0(0/5)	0.0(0/15)	NA
Linezolid	15	0	0	100.0(15/15)	100.0(15/15)	NA(0/0)	0.0(0/15)	0.0(0/15)	6.7	100.0(15/15)	100.0(15/15)	NA(0/0)	0.0(0/15)	0.0(0/15)	0.0
Rifampin	14	0	1	100.0(15/15)	100.0(15/15)	0.0(0/1)	0.0(0/14)	0.0(0/15)	0.0	100.0(15/15)	100.0(15/15)	0.0(0/1)	0.0(0/14)	0.0(0/15)	0.0
Nitrofurantoin	15	0	0	100.0(15/15)	100.0(15/15)	NA(0/0)	0.0(0/15)	0.0(0/15)	0.0	100.0(15/15)	100.0(15/15)	NA(0/0)	0.0(0/15)	0.0(0/15)	0.0
E. faecalis (n = 26)															
Penicillin	26	0	0	96.2(25/26)	100.0(26/26)	NA(0/0)	0.0(0/26)	0.0(0/26)	−27.3	92.3(24/26)	100.0(26/26)	NA(0/0)	0.0(0/26)	0.0(0/26)	23.1
Ampicillin	26	0	0	100.0(26/26)	100.0(26/26)	NA(0/0)	0.0(0/26)	0.0(0/26)	0.0	100.0(26/26)	100.0(26/26)	NA(0/0)	0.0(0/26)	0.0(0/26)	0.0

(*Continued*)

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Table 2 (Continued).

Antimicrobial	BMD			AutoMic-i600 system (%)						Vitek 2 system (%)					
	S	I	R	Agreement		Errors			Bias	Agreement		Errors			Bias
				EA	CA	VMEs	MEs	mEs		EA	CA	VMEs	MEs	mEs	
Tetracycline	5	0	21	100.0(26/26)	100.0(26/26)	0.0(0/21)	0.0(0/5)	0.0(0/26)	−14.3	100.0(26/26)	100.0(26/26)	0.0(0/21)	0.0(0/5)	0.0(0/26)	0.0
Tigecycline	26	0	0	100.0(26/26)	100.0(26/26)	NA(0/0)	0.0(0/26)	0.0(0/26)	−4.3	100.0(26/26)	100.0(26/26)	NA(0/0)	0.0(0/26)	0.0(0/26)	0.0
Erythromycin	3	9	14	96.2(25/26)	92.3(24/26)	0.0(0/14)	0.0(0/3)	7.7(2/26)	8.3	92.3(24/26)	88.5(23/26)	0.0(0/14)	0.0(0/3)	11.5(3/26)	−4.2
Ciprofloxacin	17	0	9	96.2(25/26)	96.2(25/26)	0.0(0/9)	5.9(1/17)	0.0(0/26)	5.9	100.0(26/26)	100.0(26/26)	0.0(0/9)	0.0(0/17)	0.0(0/26)	0.0
Linezolid	15	11	0	96.2(25/26)	80.8(21/26)	NA(0/0)	0.0(0/15)	19.2(5/26)	19.2	96.2(25/26)	80.8(21/26)	NA(0/0)	0.0(0/15)	19.2(5/26)	−23.1
Nitrofurantoin	26	0	0	100.0(26/26)	100.0(26/26)	NA(0/0)	0.0(0/26)	0.0(0/26)	3.8	100.0(26/26)	100.0(26/26)	NA(0/0)	0.0(0/26)	0.0(0/26)	0.0
GEH	16	0	10	NA	96.2(25/26)	0.0(0/10)	6.3(1/16)	0.0(0/26)	NA	NA	96.2(25/26)	0.0(0/10)	6.3(1/16)	0.0(0/26)	NA
STH	18	0	8	NA	96.2(25/26)	0.0(0/8)	5.6(1/18)	0.0(0/26)	NA	NA	100.0(26/26)	0.0(0/8)	0.0(0/18)	0.0(0/26)	NA
E. faecium (n = 5)															
Penicillin	0	0	5	100.0(5/5)	100.0(5/5)	0.0(0/5)	NA(0/0)	0.0(0/5)	−20.0	100.0(5/5)	100.0(5/5)	0.0(0/5)	NA(0/0)	0.0(0/5)	0.0
Ampicillin	0	0	5	100.0(5/5)	100.0(5/5)	0.0(0/5)	NA(0/0)	0.0(0/5)	0.0	100.0(5/5)	100.0(5/5)	0.0(0/5)	NA(0/0)	0.0(0/5)	0.0
Tetracycline	2	0	3	100.0(5/5)	100.0(5/5)	0.0(0/3)	0.0(0/2)	0.0(0/5)	−25.0	100.0(5/5)	100.0(5/5)	0.0(0/3)	0.0(0/2)	0.0(0/5)	0.0
Tigecycline	5	0	0	100.0(5/5)	100.0(5/5)	NA(0/0)	0.0(0/5)	0.0(0/5)	0.0	100.0(5/5)	100.0(5/5)	NA(0/0)	0.0(0/5)	0.0(0/5)	0.0
Erythromycin	0	0	5	100.0(5/5)	100.0(5/5)	0.0(0/5)	NA(0/0)	0.0(0/5)	0.0	100.0(5/5)	100.0(5/5)	0.0(0/5)	NA(0/0)	0.0(0/5)	0.0
Ciprofloxacin	0	0	5	100.0(5/5)	100.0(5/5)	0.0(0/5)	NA(0/0)	0.0(0/5)	0.0	100.0(5/5)	100.0(5/5)	0.0(0/5)	NA(0/0)	0.0(0/5)	0.0
Linezolid	5	0	0	100.0(5/5)	100.0(5/5)	NA(0/0)	0.0(0/5)	0.0(0/5)	0.0	100.0(5/5)	100.0(5/5)	NA(0/0)	0.0(0/5)	0.0(0/5)	20.0
Nitrofurantoin	0	2	3	100.0(5/5)	100.0(5/5)	0.0(0/3)	NA(0/0)	0.0(0/5)	0.0	80.0(4/5)	80.0(4/5)	0.0(0/3)	NA(0/0)	20.0(1/5)	−20.0
GEH	3	0	2	NA	80.0(4/5)	50.0(1/2)	0.0(0/3)	0.0(0/5)	NA	NA	100.0(5/5)	0.0(0/2)	0.0(0/3)	0.0(0/5)	NA
STH	3	0	2	NA	100.0(5/5)	0.0(0/2)	0.0(0/3)	0.0(0/5)	NA	NA	100.0(5/5)	0.0(0/2)	0.0(0/3)	0.0(0/5)	NA
Total (n = 79)	694	32	304	98.5(859/872)[a]	97.8(1007/1030)	1.3(4/304)	0.6(4/694)	1.5(15/1030)	1.2	97.9(854/872)[a]	97.4(1003/1030)	1.6(5/304)	0.4(3/694)	1.8(19/1030)	−5.3

Notes: [a] Cefoxitin, ICR, GEH, and STH are not included in the calculation of the EA rates because they are not applicable.

Abbreviations: NA, not applicable; S, susceptible; I, intermediate; R, resistant; SXT, trimethoprim/Sulfamethoxazole; ICR, inducible clindamycin resistance; GEH, Gentamicin high-level; STH, Streptomycin high-level.

Table 3 AutoMic-i600 System and Vitek 2 System AST Results for Isolates Found to Be Resistant to at Least One Antimicrobial Agent by the Reference BMD Method

Species (n)	AutoMic-i600 System				Vitek 2 System			
	n	EA n(%)	CA n(%)	Comment	n	EA n(%)	CA n(%)	Comment
K. pneumoniae (20)	72	71 (98.6)	71 (98.6)	1 mE with cefepime	72	67 (93.1)	64 (88.9)	1 VME with cefazolin 1 VME with cefepime 1 VME and 1 mE with aztreonam 1 mE with levofloxacin 3 mEs with nitrofurantoin
E. coli (24)	101	99 (98.0)	99 (98.0)	1 VME aztreonam 1 VME levofloxacin	101	96 (95.0)	95 (94.1)	1 mE with ampicillin 1 VME and 2 mEs with cefepime 2 mEs with levofloxacin
Enterobacter spp. (7)	17	16 (94.1)	16 (94.1)	1 mE with aztreonam	17	15 (88.2)	16 (94.1)	1 mE with nitrofurantoin
P. aeruginosa (21)	76	73 (96.1)	74 (97.4)	1 mE with imipenem 1 VME with meropenem	76	71 (93.4)	64 (84.2)	1 VME with TZP 2 mEs with cefepime 1 mE with tobramycin 2 mEs with amikacin 1 mE with levofloxacin 2 VMEs with colistin 1 mE with imipenem 2 mEs with meropenem
A. baumannii (6)	22	22 (100.0)	22 (100.0)	No errors	22	21 (95.5)	21 (95.5)	1 mE with imipenem
B. cepacia (9)	13	13 (100.0)	13 (100.0)	No errors	13	12 (92.3)	9 (69.2)	1 VME and 2 mEs with minocycline 1 mE with meropenem
S. maltophilia (7)	7	7 (100.0)	6 (85.7)	1 mE with levofloxacin	7	6 (85.7)	6 (85.7)	1 VME with ceftazidime
S. aureus (31)	106	78 (100.0)[a]	104 (98.1)	1 VME with oxacillin 1 VME with cefoxitin	106	77 (98.7)[a]	99 (93.4)	2 mEs with moxifloxacin 5 VMEs with ICR
CoNS (15)	106	80 (96.4)[a]	101 (95.3)	2 VMEs with oxacillin 1 VME with cefoxitin 1 VME with SXT 1 VME with ICR	106	78 (94.0)[a]	99 (93.4)	1 mE with gentamicin 2 mEs with moxifloxacin 1 mE with clindamycin 3 VMEs with ICR
E. faecalis (21)	62	44 (100.0)[b]	62 (100.0)	No errors	62	43 (97.7)[b]	61 (98.4)	1 mE with erythromycin
E. faecium (5)	30	26 (100.0)[b]	29 (96.7)	1 VME with GEH	30	25 (96.2)[b]	29 (96.7)	1 mE with nitrofurantoin
Total (166)	612	529 (98.1)[c]	597 (97.5)	11 VMEs, 4 mEs	612	511 (94.8)[c]	563 (92.0)	17 VMEs, 32 mEs

Notes: [a] Cefoxitin and ICR are not included in the calculation of the EA rates because they are not applicable. [b] GEH and STH are not included in the calculation of the EA rates because they are not applicable. [c] Cefoxitin, ICR, GEH, and STH are not included in the calculation of the EA rates because they are not applicable.
Abbreviations: TZP, piperacillin/tazobactam; SXT, trimethoprim/Sulfamethoxazole; ICR, inducible clindamycin resistance; GEH, Gentamicin high-level; STH, Streptomycin high level.

to cefoperazone/sulbactam, tigecycline, moxifloxacin, and ceftazidime/avibactam, as well as the sensitivity of staphylococci (n = 48) and enterococci (n = 31) to daptomycin, ceftaroline, and oritavancin.

The rates of EA (ranging from 90.3% to 100.0%), CA (ranging from 92.6% to 100.0%) and bias (ranging from −30.0 to 19.8) were acceptable for all antibiotic-pathogen combinations. Two VMEs (50%) were observed for ceftazidime/avibactam, both in *K. pneumoniae* isolates. Three MEs were observed for cefoperazone/sulbactam, two in *K. pneumoniae* isolates (6.7%), and one in an *E. coli* isolate (4.0%) (Figure 2). Besides, two VMEs were observed in staphylococci, including one for daptomycin in a *Staphylococcus haemolyticus* isolate (100.0%) and one for oritavancin in a *S. aureus* isolate (100.0%). And four MEs were noted for oritavancin, two in *S. aureus* isolates (4.3%) and two in *E. faecalis* isolates (6.5%) (Figure 3).

Discussion

Antimicrobial resistance in bacteria constitutes a worldwide challenge and poses a significant threat to public health.[26] Accurate AST is an effective means of guiding treatment strategies.[27] Broth microdilution (BMD) is the gold standard but is impractical for routine application. Current automated AST systems improve efficiency but face accuracy or operational challenges, highlighting the need for reliable and user-friendly solutions. AutoMic-i600 as a novel fully

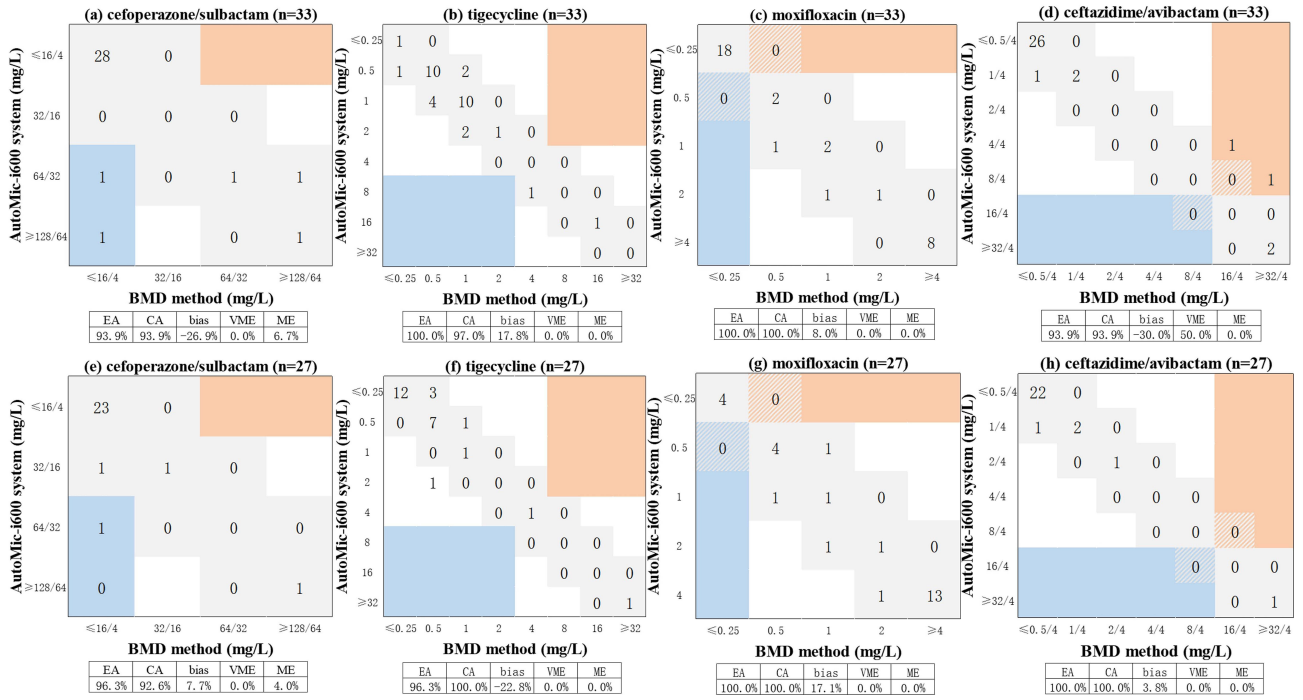

Figure 2 MICs of novel antibiotics for *K. pneumoniae* and *E. coli* using the AutoMic-i600 system compared with the BMD reference method. (**a**) Comparison of MICs obtained for cefoperazone/sulbactam-*K. pneumoniae* combination. (**b**) Comparison of MICs obtained for tigecycline-*K. pneumoniae* combination. (**c**) Comparison of MICs obtained for moxifloxacin-*K. pneumoniae* combination. (**d**) Comparison of MICs obtained for ceftazidime/avibactam-*K. pneumoniae* combination. (**e**) Comparison of MICs obtained for cefoperazone/sulbactam-*E. coli* combination. (**f**) Comparison of MICs obtained for tigecycline-*E. coli* combination. (**g**) Comparison of MICs obtained for moxifloxacin-*E. coli* combination. (**h**) Comparison of MICs obtained for ceftazidime/avibactam-*E. coli* combination. MICs corresponding to EA are in grey, VME in Orange and ME in blue. Hatching on the grey boxes within the orange (VME) and blue (ME) boxes corresponds to MICs that are also in the EA.
Abbreviations: VME, very major error; mE, minor error.

automated system based on the dual-detection of turbidimetry and colorimetry, may be a reliable new option for AST. However, few studies have evaluated the performance of the AutoMic-i600 system for susceptibility test.[18]

Here, we reported a comparison of the AutoMic-i600 and Vitek 2 systems for routine antibiotics, and also validated the detection performance of AutoMic-i600 for novel antibiotics, based on the reference BMD method. In our study, the AutoMic-i600 system performed reliably with both Gram-negative and Gram-positive bacteria, with EA rates of 93.2% and 98.5% and CA rates of 93.5% and 97.8%, respectively, which was overall equivalent (or slightly superior) to that of Vitek 2 (EA: 92.6% and 97.9%, CA: 93.5% and 97.4%, respectively). Importantly, for drug-resistant bacteria, the overall agreement of AutoMic-i600 was obviously higher than that of Vitek 2 (EA: 98.1% vs 94.8%, CA: 97.5% vs 92.0%), especially for Gram-negative bacteria (EA: 97.7% vs 93.5%, CA: 97.7% vs 89.3%). It is indicated that the AutoMic-i600 system may provide greater reliability for AST of drug-resistance bacteria compared to the Vitek 2 system. These findings align with the reports indicating the limitations of Vitek 2 in accurately testing drug-resistant strains.[28] Another commonly used AST platform, Phoenix automated system, also exhibited reduced accuracy in determining the susceptibility of CRE and MRSA isolates.[13,14] Therefore, we suggested that the AutoMic-i600 could potentially serve as a reliable and efficient new option for AST of drug-resistant bacteria.

The lower VME rate for Gram-negative bacteria with AutoMic-i600 (1.0% vs 2.9% for Vitek 2) was a notable advantage. Consistent with previous studies, we observed high VME rates with Vitek 2 for colistin in *P. aeruginosa* ((66.7%, bias = −30.8%) and cefepime in *K. pneumoniae* (20.0%, bias = −23.0%) and *E. coli* (20.0%, bias = −35.8%).[5–9] For example, recent reports have indicated that colistin testing of Gram-negative bacilli isolates by the Vitek 2 system had high rates of VME.[6,29] Jang et al similarly found that high VME rates were observed for cefepime in *K. pneumoniae* and *E. coli* with the Vitek 2 system.[7] These findings underscore the need to exercise caution when interpreting results from Vitek 2 for these antibiotics. The AutoMic-i600 system, by contrast, indicating its potential to reduce false sensitivity in drug-resistant bacteria.

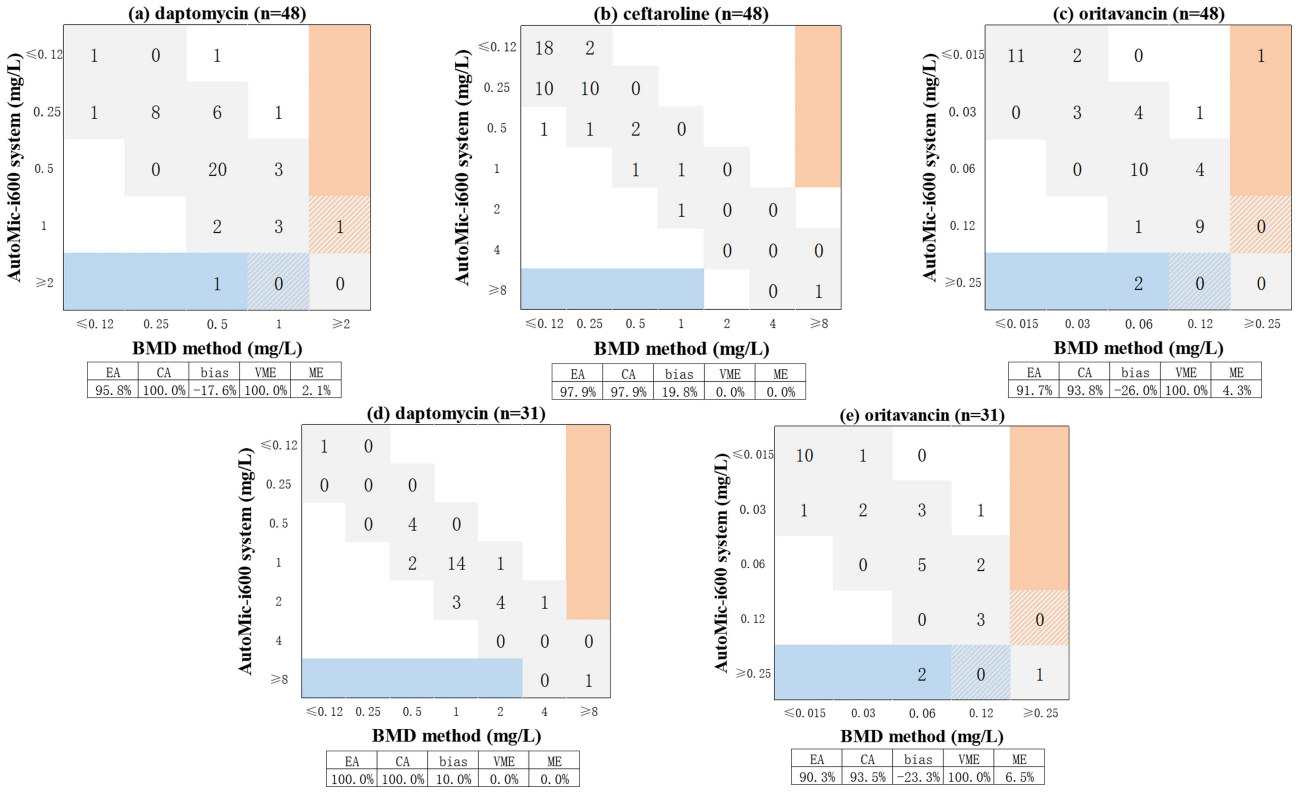

Figure 3 MICs of novel antibiotics for staphylococci and enterococci using the AutoMic-i600 system compared with the BMD reference method. (**a**) Comparison of MICs obtained for daptomycin-staphylococci combination. (**b**) Comparison of MICs obtained for ceftaroline-staphylococci combination. (**c**) Comparison of MICs obtained for oritavancin-staphylococci combination. (**d**) Comparison of MICs obtained for daptomycin-enterococci combination. (**e**) Comparison of MICs obtained for oritavancin-enterococci combination. MICs corresponding to EA are in grey, VME in Orange and ME in blue. Hatching on the grey boxes within the orange (VME) and blue (ME) boxes corresponds to MICs that are also in the EA.

Abbreviations: VME, very major error; mE, minor error.

The superior performance of AutoMic-i600 may be attributed to its dual-detection principle, which combines turbidimetry and colorimetry (four-wavelength), enabling it to detect smaller changes in bacterial growth compared to Vitek 2, which relies solely on turbidimetry (three-wavelength).[17] Furthermore, the AutoMic-i600 system covers the clinical breakpoints completely and provides directly measured MIC values, whereas the Vitek 2 system calculates the bacterial growth status by detecting 3–4 antibiotic concentrations and extrapolates the MICs based on growth kinetics, which may lead to potential calculation errors. However, the rate of ME in Gram-negative bacteria detected by AutoMic-i600 was higher than that by Vitek 2 (2.4% vs 0.9%). These false-resistant results were mainly observed for *K. pneumoniae, E. coli* and *P. aeruginosa*. We traced back these false-resistant strains and found that most were mucoid strains. The potential reason could be the insufficient grinding, resulting in the presence of tiny bacteria clumps, which might be amplified by the sensitive detection technology of AutoMic-i600. Additionally, the rates of VMEs and MEs were equivalent between the AutoMic-i600 and Vitek 2 systems in Gram-positive bacteria, which was similar to the previous study.[11]

In the context of the automated AST system, the antibiotics relatively newly incorporated into the automated AST system or approved and used in China in recent years with either under-reported or controversial performance were regarded as novel antibiotics. Specifically, ceftazidime/avibactam and oritavancin are tested for the first time in an automated AST system (ie, AutoMic-i600). Additionally, daptomycin and ceftaroline are less commonly applied in automated AST systems, and neither is included in the routine AST cards of the Vitek 2 system. Furthermore, cefoperazone/sulbactam, tigecycline, and moxifloxacin are approved and used in China for a relatively short period of time, and their performance in other automated AST systems is either under-reported or controversial.[30–32]

The inclusion of novel antibiotics brings critical new advancements to the treatment of multidrug-resistant bacteria.[33] Cefoperazone/sulbactam, tigecycline, moxifloxacin, and ceftazidime/avibactam are considered effective for treating CRE

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and ESBL-producing Enterobacteriaceae.[28,30,34,35] And daptomycin, ceftaroline, and oritavancin are reported as therapeutic options for MRSA and vancomycin-resistant enterococci (VRE).[36–38] These novel antibiotics, along with routine antibiotics, are simultaneously used for usual AST with AutoMic-i600. Compared to Vitek 2, which requires the combination of multiple AST cards, AutoMic-i600 offers a more convenient way to detect drug-resistant bacteria. In our research, the AST results of novel antibiotics by AutoMic-i600 showed high agreement with BMD (EA > 90.3%, CA > 92.6%), which could provide reliable evidence for clinical treatment decisions.

As reported previously, cefoperazone/sulbactam had high rates of error in *E. coli* by Vitek 2 (VME 40%, ME 8.5%).[30] The AutoMic-i600 system yielded no VMEs and only three MEs (*K. pneumoniae* 6.7%, *E. coli* 4.0%) for cefoperazone/sulbactam, which were much lower than those of Vitek 2. An early study has demonstrated a high rate of false non-susceptible Vitek 2 tigecycline categorization for Enterobacteriaceae and recommended the BMD method to verify such Vitek 2 results.[31] According to our research, no VMEs or MEs were noted for the tigecycline-*K. pneumoniae* and tigecycline-*E. coli* combinations. Besides, there was limited reporting on the detection performance of moxifloxacin susceptibility testing methods in Enterobacteriaceae. We found that moxifloxacin showed complete agreement between the AutoMic-i600 and BMD methods (100% EA and CA). It can be seen that the AutoMic-i600 system could serve as an effective alternative for the detection of cefoperazone/sulbactam, tigecycline, and moxifloxacin. In addition, two VMEs were noted for ceftazidime/avibactam in *K. pneumoniae*, which does not exclude the possibility of accidental error caused by the uneven distribution of certain mucoid strains.

It has been confirmed that the Vitek 2, disc diffusion, and MicroScan prompt inoculation methods are not reliable for daptomycin in enterococci, leaving laboratories with few options for testing this agent.[32] In our analysis, the AutoMic-i600 system exhibited complete agreement for daptomycin in enterococci with the BMD method (100% EA and CA). Currently, few studies have reported the detection performance of different susceptibility tests for ceftaroline in staphylococci. We found that AutoMic-i600 showed high agreement (97.9% EA and CA), and no VME or ME were observed for ceftaroline. Consequently, the AutoMic-i600 system could be considered a reliable alternative method for AST of daptomycin and cephalothin, which may perhaps make up for the shortcomings and limitations of existing AST methods. Nevertheless, one VME (*S. aureus*) and four MEs (2 of *S. aureus* and 2 of *E. faecalis*) occurred in the test with oritavancin. Although oritavancin is covered for the first time by the automated AST system, further refinement and optimisation of its detection performance are still necessary.

Potential shortcomings of this study include the possibility of accidental errors caused by insufficient grinding of mucoid strain. Also, the numbers of certain strains were limited, such as *E. faecium* and *A. baumannii* strains; further research is needed to increase the sample size and strengthen the conclusions that can be drawn.

In conclusion, the AutoMic-i600 system provides a reliable and convenient option for AST in clinical practice, particularly for drug-resistant bacteria and novel antibiotics. Its ability to achieve high agreement with BMD and reduce false sensitivity in drug-resistant Gram-negative bacteria highlights its potential to assist clinicians in making timely and accurate treatment decisions, thereby addressing the growing challenge of antimicrobial resistance.

Data Sharing Statement

Data will be made available by the author Chenyao Lin upon reasonable request.

Ethics Statement

The ethics committee of the Affiliated LiHuiLi Hospital of Ningbo University approved this study (approval number KY2023SL347-01) and waived the requirement for informed consent. This study used residual samples from the prior relevant study, which had already obtained informed consent from participants. The prior informed consent form explicitly informed participants that any remaining samples could be used for subsequent clinical research. Furthermore, all patient data and samples have been handled with strict confidentiality, in accordance with the ethical standards set forth in the Declaration of Helsinki. All data were anonymized and securely stored to ensure privacy and protect the identities of the participants.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no competing interests.

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