Evaluation of an Automated Platform for Rapid Identification and Antibiotic Sensitivity Testing of Bacteria Directly from Positive Blood Culture Bottles

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Introduction

Early diagnosis of sepsis by blood culture is a critical component of sepsis care. However, current methodology cannot provide time-critical results needed to impact early patient management. Rapid PCR-based tests are available to identify bacteria and fungi from positive blood cultures and provide predictive antibiotic susceptibility by detecting genes associated with antibiotic resistance; however, the number of organisms detected and antibiotic resistance information are limited.

The Accelerate Pheno™ system is a fully automated instrument that can detect and identify (ID) a broad range of organisms associated with sepsis and utilizes morphokinetic cellular analysis (MCA) to provide susceptibility (AST) results and MICs to an extended panel of antibiotics. IDs are available in 1.5 hours and AST results within 7 hours. This study was performed to determine the performance of this system in a hospital clinical microbiology laboratory.

Method

A total of 72 positive blood culture samples were tested on the Accelerate Pheno™ system using software v1.2 according to the manufacturer's instructions (see Figure 1). A set of 37 different Gram-positive and -negative challenge organisms were spiked into blood culture bottles with 10 mL of blood to verify the manufacturer's claims.

An additional 35 prospective clinical samples were evaluated in this study. Positive blood culture samples were inoculated onto sheep blood and MacConkey agar. Isolated colonies were identified by MALDI-TOF, and AST performed using VITEK® 2 Gram-positive and -negative panels.

Results (ID)

Of the 72 samples tested, 65 were evaluable for ID and AST performance assessment, and 7 were excluded (3 technical errors, 2 samples that were tested >8 hours post positivity, 1 kit exclusion, 1 ID failure).

Table 1: Identification Performance

Organism	Probe	Sensitivity		Specificity	
Gram-Positive					
Staphylococcus aureus	SAU	13/13	100%	51/52	98.1%
Coagulase-negative *Staph*	CNS	2/2	100%	63/63	100%
Staphylococcus lugdunensis	SLU	0/0	NA%	65/65	100%
Enterococcus faecalis	EFS	2/2	100%	63/63	100%
Enterococcus faecium	EFM	11/11	100%	54/54	100%
Streptococcus spp.	STR	3/3	100%	62/62	100%
Gram-Negative					
Escherichia coli	ECO	12/12	100%	52/53	98.1%
Klebsiella spp.	KLE	6/6	100%	58/59	98.3%
Enterobacter spp.	ENT	2/2	100%	63/63	100%
Proteus spp.	PRO	3/3	100%	62/62	100%
Citrobacter spp.	CIT	2/2	100%	63/63	100%
Serratia marcescens	SMA	1/1	100%	64/64	100%
Pseudomonas aeruginosa	PAE	4/4	100%	58/61	95.1%
Acinetobacter baumannii	ABA	1/1	100%	64/64	100%
Yeast					
Candida albicans	CAL	1/1	100%	64/64	100%
Candida glabrata	CGL	0/0	NA%	65/65	100%
Gram-Positive		**31/31**	**100%**	**358/359**	**99.7%**
Gram-Negative		**31/31**	**100%**	**484/489**	**99%**
Yeast		**1/1**	**100%**	**129/129**	**100%**
Overall		**63/63**	**100%**	**971/977**	**99.4%**

There were 2 off-panel organisms in the fresh prospective samples

Monomicrobial Call PPV: 100% (46/46)

ID demonstrated overall sensitivity of 100% and overall specificity of 99.4% vs. culture and MALDI-TOF. In addition, the system's ability to determine the monomicrobial status of the positive blood culture specimen demonstrated 100% positive predictive value (PPV) for the 46 samples where the Monomicrobial call was made.

Results (AST)

Table 2: Antimicrobial Susceptibility Testing Performance (Post-Discrepancy Testing)

Antibiotic	n	% EA	% CA	VME	ME	MiE
Gram-Positive						
Ampicillin	12	100%	100%	0	0	0
Ceftaroline*	0	NA%	NA%	0	0	0
Daptomycin	7	85.7%	100%	0	0	0
Doxycycline*	0	NA%	NA%	0	0	0
Erythromycin	10	100%	100%	0	0	0
Linezolid	21	100%	100%	0	0	0
TMP-SMX	10	100%	100%	0	0	0
Vancomycin	22	100%	100%	0	0	0
Gram-Negative						
Amikacin	30	96.7%	100%	0	0	0
Ampicillin-Sulbactam	22	100%	86.4%	0	0	3
Aztreonam	25	100%	100%	0	0	0
Cefepime	31	90.3%	87.1%	0	1	3
Ceftazidime	29	89.7%	93.1%	0	0	2
Ceftriaxone	26	100%	100%	0	0	0
Ciprofloxacin	31	100%	100%	0	0	0
Colistin*	0	-	-	0	0	0
Ertapenem	26	96.2%	96.2%	0	0	1
Gentamicin	30	100%	100%	0	0	0
Meropenem	31	100%	96.8%	0	0	1
Piperacillin-Tazobactam	29	100%	86.2%	0	0	4
Tobramycin	30	93.3%	96.7%	0	0	1
Overall	**422**	**97.4%**	**96.2%**	**0**	**1**	**15**

Results based on CLSI 2016 (M100S 26E) breakpoints
VME = Very Major Error (false-susceptibility), ME = Major Error (false-resistance),
MiE = Minor Error (one system is Intermediate (I) and the other is Susceptible (S) or Resistant (R))
**Ceftaroline, Doxycycline and Colistin were not tested by standard of care*
1 VME (Proteus spp./ampicillin-sulbactam) and 3 MEs (1 E. coli/cefepime, 1 E. coli/ceftazidime, 1 S. aureus/ erythromycin) were resolved in favor of the Accelerate Pheno™ system based on broth micro-dilution (BMD) discrepancy testing

For AST, overall Essential Agreement (EA) was 97.4% and Categorical Agreement (CA) was 96.2% when compared to VITEK® 2 results. One (1) very major error and 3 major errors were resolved in favor of the Accelerate Pheno™ system based on discrepancy testing using broth micro-dilution (BMD). The majority of minor errors were due to results that were within essential agreement and were either called Intermediate (I) or Resistant (R) by the Accelerate Pheno™ system or VITEK® 2.

Figure 1: The Accelerate Pheno™ System Workflow

Positive Blood Culture (PBC)

0.5 mL of PBC sample is loaded into sample vial and placed in reagent cartridge

Cassette and reagent cartridge with sample vial are loaded into the Accelerate Pheno™ system module and run is started

Results (Resistance & Time)

Table 3: Resistance Detection Performance

Resistance Phenotype	n	% CA	VME	ME
MRSA/MSSA (Cefoxitin & *S. aureus*)	9	100%	0/5	0/4

Table 4: Difference in Time to Results Reporting

	ID	AST
Overall Time Difference to Results (AXDX vs. SOC)	26.7 hrs	43.8 hrs

Assuming AXDX started 30 min. post positive blood culture

The Accelerate Pheno™ system demonstrated 100% categorical agreement in detecting MRSA vs. MSSA. Comparing differences in time to results reporting, there was a decrease in time to ID and AST by an average of 26.7 hours and 43.8 hours, respectively.

Conclusion

The Accelerate Pheno™ system demonstrated high performance when compared to conventional culture based ID and AST methods while significantly reducing time to results for positive blood cultures. This will allow physicians to modify treatment decisions considerably faster than with traditional methods, which should have a significant impact on patient care and antimicrobial stewardship efforts.