A Pilot Study of Accelerate PhenoTest™ BC kit (AXDX) Compared to Standard Microbiological Testing on Blood Cultures Positive for Gram-negative Bacilli

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INTRODUCTION

- Time to microbial identification (ID) and antimicrobial susceptibility testing (AST) results is a critical factor for patients with Gram-negative bloodstream infections.
- In our center, positive blood cultures containing Gram-negative bacilli (GNB) are directly tested with MALDI (DM) and the VITEK® 2 system (DV2) using a blood culture pellet.
- The Accelerate PhenoTest™ BC kit used with the Accelerate Pheno™ system (AXDX), an FDA-cleared product, is a rapid ID/AST platform which has reduced the time from positivity to microbial ID and AST results to less than 7 hours.

OBJECTIVES

- ID/AST agreement comparison of DM/DV2 to AXDX using clinical blood cultures containing GNB and blood culture samples seeded with multi-drug resistant GNB (MDR GNB).
- ID/AST time to result (TTR) comparison between AXDX, direct and conventional methods
- Proportion of clinical samples with changes to antibiotic (Abx) therapy.

METHODS

Samples

- Clinical blood cultures positive for GNB on Gram stain were collected over a three month period at our center (N=29) and sterile blood culture samples were seeded with MDR GNB (N=35, 1 GES, 4 IMP, 6 KPC, 5 NDM, 9 OXA, 4 VIM, 1 OXA/NDM, 5 non-carbapenamase). Patient characteristics, changes in antibiotics and outcomes were obtained via electronic chart review.

Testing/Comparators

- Samples were tested using AXDX (software version 1.3.1.22), DM/DV2, and compared* to conventional methods (plate incubation followed by MALDI and VITEK® 2 system).

Discrepancies

- Very major errors (VME) and major errors (ME) were confirmed with microbroth dilution.

*MICs were truncated to overlapping reportable range prior to analysis.

Figure 1: Median time to ID and AST results for clinical samples (N=29) by system run time (AXDX) or from time of blood culture positivity (Direct/Conventional).

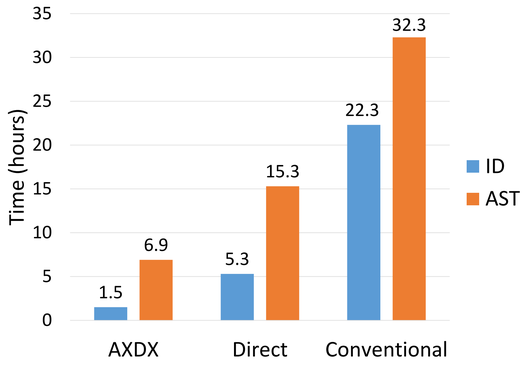

Table 1: Clinical samples - baseline characteristics and changes to antibiotics made after AST results (N=28).

Mean age	68.3
Male gender	57.1%
Diagnosis	Urosepsis (50%)
	Fever NYD (21%)
	Liver/biliary sepsis (11%)
	Other (18%)
Nosocomial bacteremia	11%
Death within 3 months	11%
Organism identified	*E. coli* (60.7%)
	K. pneumoniae (14.3%)
	K. oxytoca (7.1%)
	P. mirabilis (7.1%)
	P. aeruginosa (3.6%)
	E. cloacae (3.6%)
	C. freundii (3.6%)
Empiric antibiotics used	Ceftriaxone (62%)
	Pip/Tazo (31%)
	Ertapenem (4%)
	Meropenem (4%)
Organism resistant to empiric Abx	15%
Abx narrowed after AST results	56%

Table 2: ID Agreement Summary

Sample Type	Method	Agreement	Non-report (NR)
Clinical (N=29)	AXDX	28 (100%)	1 (3.4%)
	DM	20 (100%)	9 (32.1%)
Seeded (N=35)	AXDX	31 (93.9%)	2 (5.7%)
	DM	19 (90.5%)	14 (40%)

Table 3: AST Agreement Summary – Clinical Samples (N=28).

Method	EA	CA	VME	ME	mE	NR	Total S	Total I/R
AXDX*	292 97.0%	290 96.3%	0	0	11 3.7%	0	275	26
DV2	304 99.3%	303 99.0%	0	0	2 0.7%	2 0.6%	282	24

*AXDX only reports cefazolin for *E. coli* and *Klebsiella* spp.

Table 4: AST Agreement Summary – Seeded Samples (N=29)

AXDX

Antibiotic	EA	CA	VME	ME	mE	NR	Total S	Total I/R
Amikacin	25	25	2	0	2	0	24	5
Cefazolin*	20	20	0	0	0	1	0	20
Cefepime	24	22	1	0	6	0	7	22
Ceftazidime	28	26	0	0	3	0	2	27
Ceftriaxone	27	26	0	0	2	1	3	25
Ciprofloxacin	29	27	0	0	2	0	3	26
Ertapenem	24	23	2	0	2	2	5	22
Gentamicin	27	26	0	0	3	0	15	14
Meropenem	13	14	0	0	0	15	1	13
Pip/Tazo	27	25	0	0	4	0	4	25
Tobramycin	28	26	0	0	3	0	7	22
TOTAL (%)	272 93.2%	260 89.0%	5 2.2%	0	27 9.2%	20 6.4%	71	221

Direct VITEK® 2 system

Antibiotic	EA	CA	VME	ME	mE	NR	Total S	Total I/R
Amikacin	28	27	1	0	1	0	22	7
Cefazolin	29	29	0	0	0	0	0	29
Cefepime	28	27	0	0	2	0	12	17
Ceftazidime	29	29	0	0	0	0	3	26
Ceftriaxone	28	28	0	0	1	0	2	27
Ciprofloxacin	29	29	0	0	0	0	3	26
Ertapenem	28	28	1	0	0	0	3	26
Gentamicin	29	27	0	0	3	0	15	14
Meropenem	25	23	1	0	4	1	6	22
Pip/Tazo	28	27	0	0	2	0	3	26
Tobramycin	29	28	0	0	1	0	7	22
TOTAL (%)	310 97.5%	302 94.7%	3 1.3%	0	14 4.4%	1 0.3%	76	242

*AXDX only reports cefazolin for *E. coli* and *Klebsiella* spp.

Abbreviations: CA=categorical agreement; EA=essential agreement; I=intermediate; mE=minor error; ME=major error; NR=non-report; Pip/Tazo=piperacillin-tazobactam; R=resistant; S=susceptible; VME=very major error.

MICs were truncated to overlapping reportable range prior to analysis.

RESULTS

Timing & Antibiotic Optimization

- Time to result (TTR) in Figure 1 reflect system run times for AXDX and clinical TTR for direct/conventional methods
- Antibiotic therapy was broadened for 15% of patients and narrowed for 56% based on ID/AST results (Table 1)

ID Agreement

- AXDX and DM overall agreement were both >90% (Table 2)
- DM had a high ID non-report rate for clinical and seeded

AST Agreement

- Clinical overall EA/CA were >96% for both AXDX and DV2; there were no VME or ME and mE was <4%
- Seeded EA/CA were lower for AXDX compared to DV2
- AXDX had a high meropenem non-report rate for seeded, which will be addressed in a future software release

Limitations

- The comparator, conventional VITEK® 2, is not a gold-standard method
- Small sample size

CONCLUSIONS

- AXDX was more than 50% faster than DM/DV2
- DM and DV2 was more than 4x and 2x faster than conventional MALDI and VITEK® 2 system, respectively
- AST results from 15% of clinical samples would have had critical impact by identifying organisms resistant to empiric antibiotics
- DM/DV2 and AXDX both had high agreement with clinical samples
- DV2 had higher agreement than AXDX when challenged with multi-drug resistant organisms

FUTURE DIRECTION

- Before and after study comparing the clinical and financial impact of DM compared to conventional MALDI
- Before and after study comparing the clinical and financial impact of DV2 compared to DM and conventional VITEK
- Explore value & impact of higher ID report rates with AXDX

CONTACT INFORMATION

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