Evaluation of the Accelerate *pheno*™ System versus current blood culture ID/AST methods and potential impact on antimicrobial stewardship and patient management

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BACKGROUND/INTRODUCTION

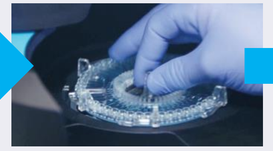
The rise in antimicrobial resistance has prompted a call for rapid antimicrobial susceptibility testing (AST) strategies to be investigated, particularly those for bacteraemia[1]. New advancements could significantly impact antimicrobial stewardship, patient management and outcomes[2]. Timely AST results are critical to determining targeted treatment regimens for septic patients[3]. Our laboratory uses BSAC disc diffusion methods[4] directly on positive blood cultures and identification (ID) confirmation and MIC determination via the bioMeriéux Vitek2®. These methods, despite being accurate, are relatively laborious and time consuming. A rapid alternative for septic patients is needed.

We have completed an initial evaluation of the Accelerate PhenoTest™ BC Kit on the novel Accelerate *pheno*™ system. We compared the rapid pathogen ID and MIC-AST that the PhenoTest™ produced via fluorescent *in situ* hybridisation and morphokinetic cellular analysis with our current standard of care (SoC). Gram negative (GN) infections were of particular interest due to greater unpredictability of susceptibility patterns and as such, a more timely intervention compared to current SoC could potentially carry a significant impact on patient management.

METHODS

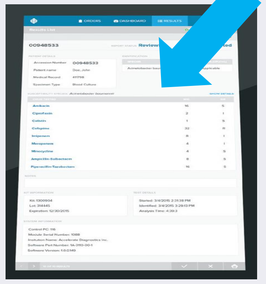
The decision to run the Accelerate PhenoTest™ BC assay was at the discretion of the consultant microbiologist once predefined criteria had been met; of a clinically septic patient in the emergency department or intensive care unit with an organism visualised on Gram stain. **53** eligible samples from **51** unique patients were tested.

Positive BC was added to sample vial and inserted into reagent cartridge.



The cassette was loaded and locked in place.

The reagent cartridge was loaded and START engaged.



Key performance indicators:

- Time to Accelerate PhenoTest™ BC pathogen ID and MIC-AST v current SoC
- Subsequent impact on patient care:
  - *In vitro* to oral antibiotic switch
  - Reduction of the use of meropenem and piperacillin-tazobactam (Tazocin)
  - Infection prevention/control (IPC) interventions

We hope to assess these data to see if it will help us meet two of the 2016/17 NHS England CQUIN[5] goals: 1) ID and early treatment of Sepsis 2) Antimicrobial resistance

RESULTS

The Accelerate PhenoTest™ BC kit ID produced a sensitivity of **90.6%** and a specificity of **99.8%** (Table 1) within **1 hour 25 minutes** vs SoC at **12-24 hours**. The **34** runs eligible for AST analysis showed **97.0%** essential agreement (EA) and **96.3%** categorical agreement (CA) (Table 2) compared to SoC. MIC results were reported within **7 hours** of a positive BC on the PhenoTest™ vs SoC AST at **24 hours** and MIC at **48 hours**.

In **53** runs the Accelerate Pheno™ system showed only **3** system failures and **50** valid results. Antibiotic susceptibility by MIC was not reported in only **3/39** AST eligible runs (**1** analysis failure, **1** mechanical failure, **1** with too many clones in the growth channel). **2** SoC runs had incomplete data as they were fully sensitive organisms, no further value would have been gained from Vitek2® analysis.

ID Results	SN		SP	
Gram-Positives				
CoN Sta spp.	4/4	100%	47/47	100%
EntFM	1/1	100%	49/49	100%
EntFS	2/2	100%	48/48	100%
StrAG			50/50	100%
StaAU	8/9	89%	41/41	100%
StaLU			50/50	100%
Str spp.	2/2	100%	48/49	98%
Gram-Negatives				
AcBA			50/50	100%
CIT spp.			50/50	100%
ECO	18/21	86%	29/29	100%
ENTB spp.	0/1	0%	49/49	100%
KLEB spp.	10/10	100%	40/40	100%
PYO	1/1	100%	49/49	100%
PRO spp.			50/50	100%
SMARC	2/2	100%	48/48	100%
Yeast				
CALB			50/50	100%
CGLA			49/50	98%
Total	**48/53**	**90.6%**	**849/851**	**99.8%**

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AST Results	EA		CA		VMD	MAJ	MIN
Gram-Positives							
AMP	-	-	-	-	-	-	-
CFT	-	-	-	-	-	-	-
DAP	-	-	-	-	-	-	-
DOX	-		5/6		-	-	1
ERY	1/2		6/6		-	-	-
FOX	NA		5/6		-	1	-
LZD	-		7/7		-	-	-
MLSB	NA		5/6		-	1	-
SXT	-		1/1		-	-	-
VAN	-		2/2		-	-	-
Gram-Negatives							
AMK	18/19	-	21/21	-	-	-	-
ATM	-	-	-	-	-	-	-
CAZ	-	-	-	-	-	-	-
CFZ	-	-	-	-	-	-	-
CIP	19/19	-	27/27	-	-	-	-
CRO	18/18	-	25/26	-	-	-	1
CST	1/1	-	1/1	-	-	-	-
ETP	18/18	-	19/19	-	-	-	-
FEP	18/18	-	16/19	-	-	-	3
GEN	18/18	-	26/26	-	-	-	-
MEM	16/19	-	26/27	-	-	-	1
SAM	-	-	-	-	-	-	-
TOB	16/17	-	16/17	-	-	1	-
TZP	17/17	-	25/25	-	-	-	-
Total	**159/164**	**97.0%**	**235/244**	**96.3%**	**-**	**3**	**6**

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DISCUSSION/CONCLUSIONS

In this limited evaluation, early ID and AST using the Accelerate PhenoTest™ BC Kit facilitated **5** escalations of treatment, **3** *in vitro* to oral antibiotic switches, **2** early infection prevention interventions and early cessation of broad-spectrum antibiotic (Tazocin) in some cases which represents a start to meeting appropriate CQUIN targets.

Rapid pathogen AST was particularly useful for patients infected with GN organisms, with less predictable antibiograms, where optimal therapy differed from our NHS Trust's empirical sepsis treatment regime of amoxicillin and gentamicin. This allowed for potential optimisation of antimicrobial therapy at 7 hours versus 24 hours, but due to the antibiotic panel on the PhenoTest™ BC Kit being US-focused (Table 2), at this time, we could not fully explore this as comparisons with SoC MICs were not comprehensive, especially when encountering ESßLs. The Accelerate *pheno*™ system within our NHS Trust has potential to seamlessly augment our SoC and allow for early targeted management of patients with sepsis. Considering the throughput of the Accelerate *pheno™* system and additional investment requirements we would target only those septic patients where a rapid ID and phenotypic AST result would have the greatest potential impact on patient care.

The Accelerate *pheno™* system represents an exciting development to facilitate responsive directed antimicrobial therapy to improve patient outcomes, especially in light of increasingly unpredictable resistance patterns that are being encountered more frequently clinically.

A second phase of the trial to assess its use in 24/7 clinical practice begins May 2017 with funding in place for a cohort of 30 patients.

REFERENCES

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5. Commissioning for Quality and Innovation (CQUIN), *Department of Health*, Guidance 2016/17