Performance and diagnostic accuracy of Accelerate Pheno™ system on clinical blood cultures in diagnosis of bacteremia

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#P115

Background-Aims

In severe sepsis, inappropriate therapy can be associated with adverse effects, reducing the patient's survival. Substantial progress has been made in reducing time-to results for microbial identification (ID) and antimicrobial susceptibility testing (AST), which can significantly reduce the number of adverse effects and the costs of empirical broad-spectrum treatments. Accelerate Pheno™ system (AXDX) is an automated platform that uses single-cell analysis technology to rapidly identify pathogens and provide information on antibiotic susceptibility (approximately 7 hours) directly from positive blood culture (BCs). To evaluate the performance of the Accelerate Pheno™ system compared to routine diagnostic techniques, the Microbiology Department of Synlab Ticino, in collaboration with Clinica Luganese Moncucco, Lugano, has performed a pilot study using positive BCs from patients with bacteremia or sepsis.

Methods

The Accelerate Pheno™ system (AXDX; Accelerate Diagnostics, USA) is a fully automated system that combines fluorescence in situ hybridization (FISH) for ID and time-lapse microscopy and bacterial growth rates to determine MIC values. During a 3-months period (July-September 2017), 47 positive BCs, corresponding to unique episodes of BSI, were analyzed both by AXDX and conventional methods, which included MALDI-TOF (Bruker) for ID and automated system (BD Phoenix) and disk diffusion (Kirby-Bauer) for AST. Results were interpreted according to EUCAST guidelines (v 6.0). Comparisons between AXDX and conventional methods for AST are reported as essential agreement (EA), categorical agreement (CA), very major error (VME - false susceptibility), major error (ME - false resistance), or minor error (MiE - intermediate versus susceptible or resistant).

Figure 1: *Technology overview Accelerate Pheno™ system*

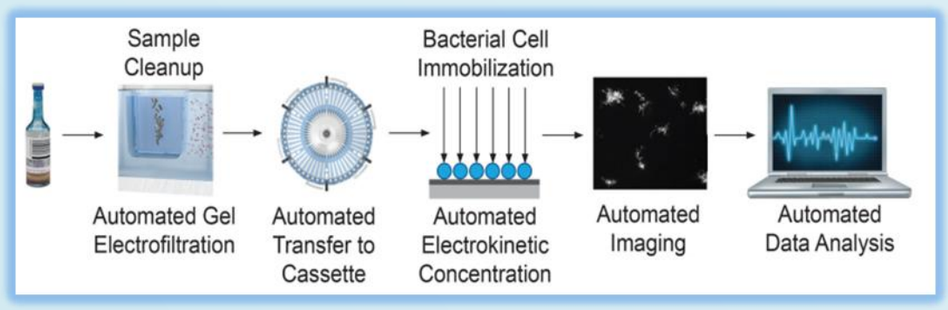


Figure 2a: *Distribution of positive blood culture by ward*

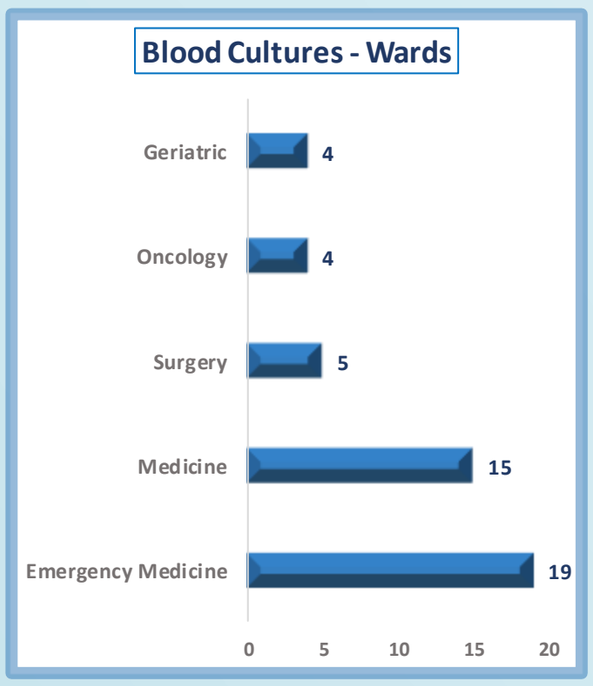
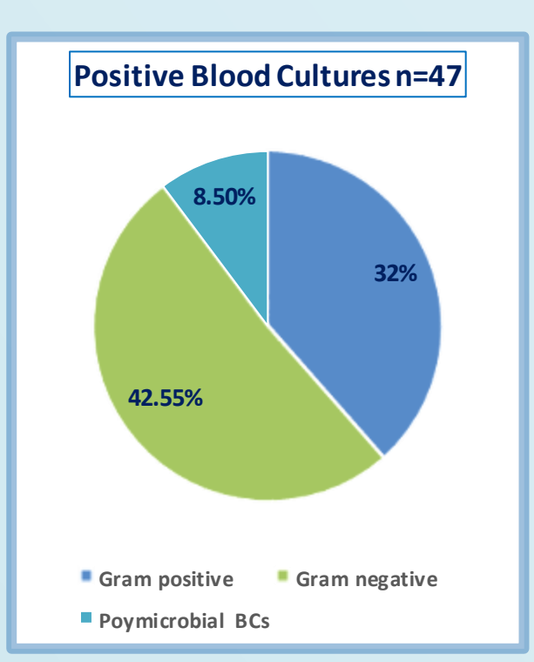


Figure 2b: *Distribution of positive blood culture by organism*

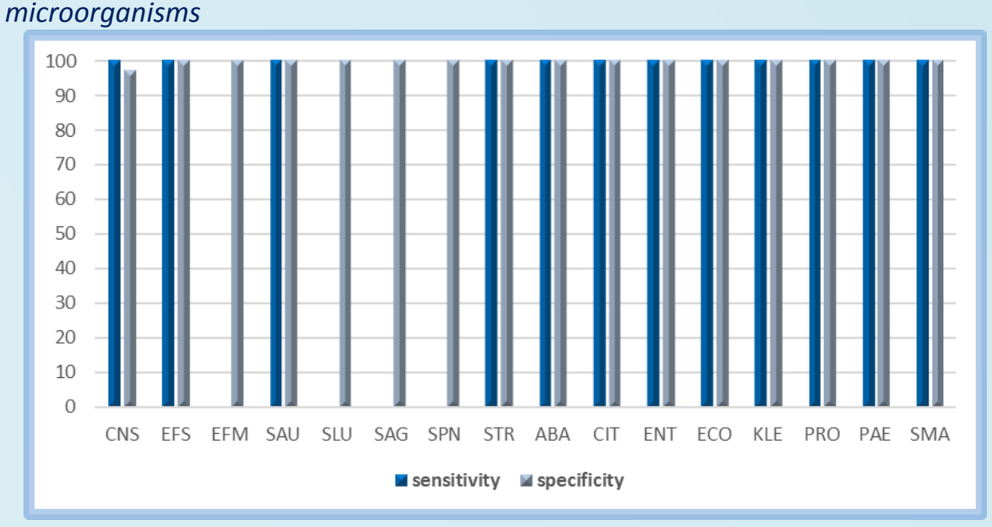


Results

Identification Results

Overall of 47 BCs were run on AXDX. The instrument detected 22 Gram negative, 14 Gram positive and 3 off-panel microorganisms which were identified by conventional method as *Salmonella napoli, Enterococcus gallinarum, Stenotrophomonas maltophilia*. Six samples were excluded: 3 technical failures, 2 ID negative reports linked to too few bacterial cells in blood (*Asaia bogorensis* and *Lactobacillus sakei)*, 1 ID partial report in a polymicrobial sample where AXDX could provide identification for *E.coli* only but not for *K.oxytoca*. The proportion of organisms in this study for which a result was obtained using AXDX was 87.8%. AXDX provided 99.8% correct identification related to on panel microorganisms.

Figure 3: *Identification Performance: Gram-positive and Gram-negative microorganisms*



Susceptibility Results

Concerning AST testing, a total of 270 microorganism-antimicrobial combinations were analyzed and compared to the culture-based AST results of Phoenix. The overall EA was 94.1%, the CA 92,8%. A low CA was observed for cefepime (85.0%), ceftazidime (88.9%), ciprofloxacin (80.0%) and colistin (84.2%) in Gram negative microorganisms. Discrepancies were linked to VME (5.9%), ME (3.7%) and MiE (3.4%). The median ID run time was 1.5 h and the average time for Accelerate Pheno™ system to provide ID/AST was 6:21 h, with results available in 29h before culture-based-methods.

Table1a: *AST Performance for Gram-Positive Organisms*

ANTIBIOTIC	EA[1]		CA		VME	ME	MiE
Ampicillin	3/3	100%	3/3	100%	0	0	0
Daptomycin	9/11	81.8%	8/8[2]	100%	0	0	0
Erythromycin	7/8	87.5%	7/8	87.5%	0	1 (20%)	0
Linezolid	9/11	81.8%	11/11	100%	0	0	0
Trimethoprim-Sulfamethoxazole	2/2	100%	2/2	100%	0	0	0
Vancomycin	10/11	90.9%	11/11	100%	0	0	0
Total	40/46	87.0%	42/43	97.7%	0	1	0

[1]Results are calculated based on EUCAST 2016 breakpoints and compared with" truncated reportable ranges"
[1] 3/11 included in EA were excluded from CA because no breakpoints were specified for 3 *Enterococcus faecalis*.

Table1b: *AST Performance for Gram-Negative Organisms*

ANTIBIOTIC	EA[1]		CA		VME	ME	MiE
Amikacin	20/20	100%	20/20	100%	0	0	0
Aztreonam	15/17	88.2%	15/17	88.2%	0	0	2 (11.8%)
Cefepime	20/20	100%	17/20	85.0%	0	1 (6.3%)	2 (10.0%)
Ceftazidime	17/18	94.4%	16/18	88.9%	0	1 (6.3%)	1 (5.6%)
Ceftriaxone	16/17	94.1%	16/17	94.1%	1 (33.3%)	0	0
Ciprofloxacin	20/20	100%	16/20	80.0%	0	0	4 (20.0%)
Colistin	16/19	84.2%	16/19	84.2%	0	3 (15.8%)	0
Ertapenem	17/17	100%	17/17	100%	0	0	0
Gentamicin	16/18	88.9%	16/18	88.9%	0	2 (11.8%)	0
Meropenem	20/20	100%	20/20	100%	0	0	0
Piperacillin-Tazobactam	19/20	95.0%	17/18[2]	94.4%	0	1 (5.6%)	0
Tobramycin	18/18	100%	18/18	100%	0	0	0
Total	214/224	95.5%	204/222	91.9%	1	8	9

[1]Results are calculated based on EUCAST 2016 breakpoints and compared with" truncated reportable ranges"
[2] 2/20 included in EA were excluded from CA because no breakpoints were specified for 2 *Acinetobacter baumannii.*

Conclusions

The Accelerate Pheno™ system accurately detects resistance phenotypes of microorganisms responsible for BSIs and provides fast reliable ID results in in less than 90 minutes, and most importantly, reliable AST results in less than 7 hours from the detection of a positive blood culture. According our experience, further studies are needed to improve the AST assay due to observation of discrepancies for some antibiotics compared to routine method. Additionally, before the AXDX system is fully implemented, a cost analysis and the impact of fast results on clinical outcomes need to be assessed.

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