Accelerating Time to Pathogen-adapted Antibiotic Treatment by Subculture-independent Antimicrobial Susceptibility Testing in Patients suffering from Sepsis

Matthias Karrasch[1], Marco Bender[1], Jennifer Geraci[1], Bettina Löffler[1], Jürgen Rödel[1]

[1]Institute of Medical Microbiology, Jena University Hospital, Jena, Germany

Introduction:

- accurate & fast pathogen identification with consecutive antimicrobial susceptibility testing (AST) is of vital importance for patients suffering from sepsis.

Methods:

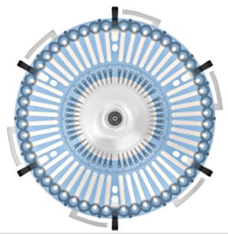
- the Accelerate Pheno™ system is a new, fully automated, subculture-independent diagnostic method for both pathogen identification (ID) and antimicrobial susceptibility testing (AST) from positive blood culture bottles.
- we analyzed positive blood cultures from critically ill patients with new onset of sepsis, using both conventional standard methods (VITEK, MALDI-TOF) and the Accelerate Pheno™ system.
- Accelerate Pheno™ ID/AST results were not reported to treating physicians as part of our internal evaluation process.

S. aureus
S. lugdunensis
CoNS spp.
E. faecium
E. faecalis
Streptococcus spp.
E. coli
Klebsiella spp.
Enterobacter spp.
Proteus spp.
Citrobacter spp.
S. marcescens
P. aeruginosa
A. baumannii
C. albicans
C. glabrata

48 Channels allow multiple assays

20 flow channels for ID

28 flow channels for AST

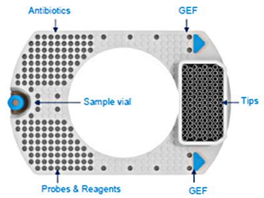


Multipurpose reagent cartridge design

100 pipette tips

Over 150 wells for antimicrobials, media, reagents, probes, and waste

2 Gel Electro-Filtration wells for sample prep



Results (1):

ID Performance for 89 evaluable organisms: sensitivity: 96,4%, specificity: 99,8%

Gram-negative pathogens	T	TP	FP	FN	TN (= 89-T)	Sensitivity (=TP/(TP+FN)	Specificity (=TN/(TN+FP)
E. coli	43	41	1	1	46	97,6%	97,9%
P. aeruginosa	3	3	0	0	86	100%	100%
Klebsiella spp.	6	6	0	0	83	100%	100%
Proteus spp.	4	3	0	1	85	75%	100%
Enterobacter spp.	3	3	0	0	86	100%	100%
A. Baumanii	2	2	0	0	87	100%	100%
Citrobacter spp.	0	0	0	0	89	NA	100%
Total GN	**61**	**58**	**1**	**2**	**473**	**96,7%**	**99,8%**

Gram-positive pathogens	T	TP	FP	FN	TN (= 89-T)	Sensitivity (=TP/(TP+FN)	Specificity (=TN/(TN+FP)
Ent. faecalis	4	4	0	0	85	100%	100%
Ent. faecium	4	3	0	1	85	75%	100%
CNS	11	11	0	0	78	100%	100%
S. aureus	4	3	1	0	85	100%	98,8%
Streptococcus spp.	1	1	0	0	88	100%	100%
Total GP	**24**	**22**	**1**	**1**	**421**	**95,7%**	**99,8%**

definitions & abbreviations: GN: Gram negative; GP: Gram positive; T: total number; TP: true positive; FP: false positive; FN: false negative; TN: true negative; AXDX: Accelerate; EA: essential agreement (EA): MIC result obtained with the AST device that is within plus or minus one doubling dilution step from the MIC value established with the reference method (ISO 20776-1); CA: categorical agreement [agreement of SIR results between a breakpoint test or an MIC test and the reference method (ISO 20776-1)]; error definitions: minor error: MIC discrepancy >1 dilution level or categorical discrepancy between S/I or R/I; major error: AXDX: R and SOC: S; minor error: AXDX: S and SOC: R

Results (2):

Antibiotic Agents Against Gram-negative pathogens	Count (EA/CA)	EA	CA
Ampicillin/Sulbactam	43	81,4% (35/43)	93% (40/43)
Piperacillin/Tazobactam	49/50	91,8% (45/49)	86% (43/50)
Ceftazidime	51/52	92,2% (47/51)	90,4% (47/52)
Ceftriaxone/Cefotaxime	48	N/A*	97,9% (47/48)
Ertapenem	49	93,9% (46/49)	100% (49/49)
Meropenem	53/54	94,4% (50/53)	96,3% (52/54)
Gentamicin	51	96,1% (49/51)	96,1% (49/51)
Ciprofloxacin	53/54	94,3% (50/53)	94,4% (51/54)
Amikacin	2	50% (1/2)	100% (2/2)
Tobramycin	2	100% (2/2)	100% (2/2)
Aztreonam	2	50% (1/2)	100% (2/2)
Colistin	2	100% (2/2)	100% (2/2)

Antibiotic Agents Against Gram-positive pathogens	Count (EA/CA)	EA	CA
Ampicillin	7	100% (7/7)	100% (7/7)
Linezolid	14/15	100% (14/14)	100% (15/15)
Vancomycin	13/17	100% (13/13)	100% (17/17)
Doxycycline	0/6	N/A*	100% (6/6)
Daptomycin	6	83,3% (5/6)	100% (6/6)
Trimethoprim/ Sulfamethoxazol	2	0% (0/2)	100% (2/2)
Methicilin-Resistance screen	7	N/A	100% (7/7)
MLSB screen	2	N/A	100% (2/2)

AST Performance for 74 evaluable organisms:
- EA: 91,7%
- CA: 95,5%

Overall AST Error Rate:
- minor error: 5,7% (27/471)
- major error: 1,5% (7/471)
- very major error: 0,6% (3/471)

Organism	Ø ID-Time AXDX	Ø AST-Time AXDX	Ø ID-Time SOC	Ø AST-Time SOC	Δ ID-Time	Δ AST-Time
E. coli	1,3	6,6	19,6	30,9	18,2	24,3
P. aeruginosa	1,4	6,6	7,0	31,0	5,6	24,4
Klebsiella spp.	1,4	6,6	23,2	31,5	21,9	24,9
Proteus spp.	1,3	6,6	23,3	32,1	22,0	25,5
Enterobacter spp.	1,4	6,6	17,2	33,3	15,8	26,7
A. baumanii	1,4	6,5	24,8	33,5	23,4	27,0
	1,37	**6,58**	**19,18**	**32,05**	**17,82**	**25,47**

average time to result reduction for GN:
- ID: 17,82 hours
- AST: 25,47 hours

Organism	Ø ID-Time AXDX	Ø AST-Time AXDX	Ø ID-Time SOC	Ø AST-Time SOC	Δ ID-Time	Δ AST-Time
Ent. faecalis	1,3	6,5	12,9	33,0	11,5	26,5
Ent. faecium	1,4	6,5	7,3	30,4	6,0	24,0
CNS	1,3	6,5	13,2	32,3	11,8	25,9
S. aureus	1,4	6,5	9,3	33,3	8,0	26,7
	1,35	**6,50**	**10,68**	**32,25**	**9,33**	**25,78**

average time to result reduction for GP:
- ID: 9,33 hours
- AST: 25,78 hours

average time to result reduction (GP+GN):
- ID: 14,42 hours
- AST: 25,59 hours

Conclusion:

- Accelerate Pheno™ system significantly improved time-to-ID/AST when compared to standard methods.
- Due to the short hands-on-time, subculture-independence, and fast generation of results, this system represents a promising new diagnostic method for pathogen-adapted antibiotic treatment in selected patients
- ID/AST results would have led to a reduced time-to-treatment, if reported. System could thus serve as an innovative antibiotic stewardship (ABS) diagnostic tool.
- Accelerate Pheno™ system is not yet applicable for a high throughput of patient samples, preselection of critical patient specimens within a routine microbiology laboratory setting is needed.
- Microbiology laboratories should independently evaluate how this system fits into their workflow and their patient population, based on a risk stratification.

Acknowledgements:
- Special thanks to Natalia Duarte, Roman Hopkins and Violetta Lomakowskaja from Accelerate Diagnostics for the training and technical support.

Session: 237: Novel Diagnostics; Saturday, October 7, 2017; 12:30 p.m. - 2 p.m. poster board number: 2089

October 4-8 • San Diego, CA • www.idweek.org
IDWeek 2017™