Evaluation of the ASTar® system for Rapid Susceptibility Testing Directly from Positive Blood Cultures from Oncology Patients with Bloodstream Infections

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Abstract (Updated)

Background: Immunocompromised patients have an increased risk of sepsis. Failure to administer effective therapy within the first 24 h of sepsis onset is associated with high mortality rates. The ASTar® system is a fully automated instrument for rapid antimicrobial susceptibility testing (AST) directly from positive blood cultures. It prepares an inoculum for AST and determines the minimal inhibitory concentration for each antimicrobial with high-speed time-lapse microscopy imaging of organisms in broth microdilution (BMD). This study aimed to evaluate the performance of the ASTar® system for Gram-negative rod (GNR) positive blood cultures in a clinical setting.

Methods: Monomicrobial positive blood cultures from unique patients were included in this study. The ePlex® Blood Culture Identification (BCID) Gram-negative panel was used to identify the GNR organisms. The ASTar® panel was performed according to manufacturer's instructions and organisms were tested across 18 antimicrobials: amikacin, ampicillin, ampicillin/sulbactam, aztreonam, cefazolin, cefepime, ceftazidime, cefuroxime, ceftazidime/avibactam, ciprofloxacin, gentamicin, levofloxacin, meropenem, meropenem/vaborbactam, piperacillin/tazobactam, tobramycin, tigecyline, and trimethoprim/sulfamethoxazole. Categorical agreement (CA), minor errors (mE), major errors (ME) and very major errors (VME) and essential agreement (EA) were calculated using the standard of care, automated BMD on the Microscan WalkAway, as comparison method.

Results: A total of 61 positive bloods for the following organisms were included: *Escherichia coli* (n=19), *P. aeruginosa* (n=9), *K. pneumoniae* (n=20), *K. oxytoca* (n=1), *K. aerogenes* (n=1) *Proteus mirabilis* (n=2), *Serratia marcescens* (n=1), *Citrobacter freundii* (n=1) and *Enterobacter cloacae* complex (n=7). Low CA was observed for cefazolin (65%), followed by ampicillin-sulbactam (81%) while all other antimicrobials had CAs ranging from 90-100%. Most errors observed were mEs, with an overall rate of 4%, ME rate was 1% and VME rate was 1%. Overall, EA was 96%, with most antimicrobials being acceptable.

Conclusion: Results suggest that the ASTar® system yields reliable AST results with an overall CA of 94% and 96% EA. The ASTar® system combined with direct from positive blood rapid identification can help in the optimization of early antimicrobial therapy in patients with bloodstream infections.

Background

- Failure to administer effective therapy within the first 24 h of sepsis onset is associated with high mortality rates.
- The ASTar® system is a fully automated instrument for rapid AST directly from positive blood cultures.
- The system is currently FDA cleared for the organism and antimicrobials listed on **Table 1**.

Antimicrobial class	Antimicrobial agent	*A. baumannii*	*C. freundii*	*C. koseri*	*E. cloacae* complex	*E. coli*	*K. aerogenes*	*K. oxytoca*	*K. pneumoniae*	*P. aeruginosa*	*P. mirabilis*	*P. vulgaris*	*S. marcescens*
Penicillins	Ampicillin					•					•		
β-lactam combination agents	Ampicillin-sulbactam[1]					•		•	•		•	•	
	Ceftazidime-avibactam[2]		•	•	•			•		•	•		•
	Meropenem-vaborbactam[3]		•	•	•	•	•	•	•		•		•
	Piperacillin-tazobactam[4]			•		•			•		•	•	•
Cephalosporin	Cefazolin								•				
	Cefepime		•			•	•	•	•	•	•	•	•
	Cefuroxime					•		•	•		•		
	Ceftazidime				•	•		•	•		•	•	•
Monobactam	Aztreonam			•	•	•	•	•	•		•	•	•
Carbapenem	Meropenem	•	•	•		•				•	•	•	•
Aminoglycoside	Gentamicin		•	•				•	•	•	•	•	•
	Tobramycin		•	•	•	•			•		•		•
	Amikacin		•		•		•	•	•	•	•		•
Tetracycline	Tigecycline		•	•	•	•	•	•	•				•
Fluoroquinolone	Ciprofloxacin			•	•	•	•	•	•	•	•	•	•
	Levofloxacin		•	•	•	•	•	•	•	•	•	•	•
Miscellaneous	Trimethoprim-sulfamethoxazole[5]				•	•	•	•	•			•	

[1] Ampicillin-sulbactam in the ratio 2:1
[2] For susceptibility testing purposes, the concentration of avibactam is fixed at 4 µg/mL
[3] For susceptibility testing purposes, the concentration of vaborbactam is fixed at 8 µg/mL
[4] For susceptibility testing purposes, the concentration of tazobactam is fixed at 4 µg/mL
[5] Trimethoprim-sulfamethoxazole in the ratio 1:19

Table 1. FDA-cleared combinations

Methods

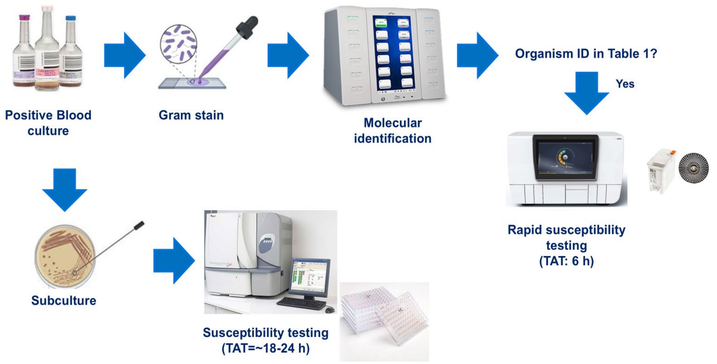

Figure 1. Laboratory workflow

- This was a prospective study conducted at Memorial Sloan Kettering Cancer Center.
- Positive blood cultures with Gram-negative organisms in **Table 1** identified by the ePlex® Gram-negative panel were included in this study.
- Only one isolate per patient was included.
- Categorical agreement (CA), minor errors (mE), major errors (ME) and very major errors (VME) and essential agreement (EA) were calculated using the standard of care, automated BMD on the Microscan WalkAway, as comparison method.
- Discrepant analysis was performed by repeating AST of the isolates on the MicroScan and by spiking them into blood culture bottles to repeat the ASTar®.

Results

Organism	N	ESBL	CRE*	MDR
Escherichia coli	19	5	1	
Klebsiella pneumoniae	20	4	1	
Enterobacter cloacae complex	7		2	
Klebsiella oxytoca	1			
Serratia marcescens	1			
Pseudomonas aeruginosa	9			2**
Klebsiella aerogenes	1		1	
Proteus mirabilis	2			
Citrobacter freundii	1			
Acinetobacter baumanii	0			
Citrobacter koseri	0			
Proteus vulgaris	0			
Total	**61**	**9**	**5**	**2**

Table 2. Organisms included

*Spiked **1 spiked MDR
ESBL= Extended spectrum beta-lactamase
CRE= Carbapenem resistant Enterobacterales
MDR= Multidrug resistant

Antimicrobial	EA	N	%	CA	N	%	S	I	R	mE	%	ME	%	VME	%
Ampicillin	21	21	100%	20	21	95%	5	1	15	1	5%	-	-	-	-
Ampicillin-sulbactam	41	42	98%	34	42	81%	25	6	11	8	19%	-	-	-	-
Meropenem-vaborbactam	52	52	100%	52	52	100%	52	-	-	-	-	-	-	-	-
Piperacillin-tazobactam	37	42	88%	38	42	90%	39	1	2	2	5%	2	5%	-	-
Cefepime	51	54	94%	51	54	94%	38	1	15	3	6%	-	-	-	-
Cefuroxime	41	42	98%	41	42	98%	26	2	14	1	2%	-	-	-	-
Ceftazidime	49	50	98%	47	50	94%	33	2	15	3	6%	-	-	-	-
Aztreonam	51	51	100%	50	51	98%	36	1	14	1	2%	-	-	-	-
Meropenem	32	32	100%	32	32	100%	29	-	3	-	-	-	-	-	-
Tobramycin	50	50	100%	46	50	92%	44	2	4	4	8%	-	-	-	-
Tigecycline	49	50	98%	49	50	98%	49	1	-	1	2%	-	-	-	-
Ciprofloxacin	60	60	100%	57	60	95%	42	2	16	3	5%	-	-	-	-
Levofloxacin	61	61	100%	58	61	95%	43	4	14	3	5%	-	-	-	-
Trimethoprim-sulfamethoxazole	47	48	98%	47	48	98%	28	-	20	-	-	1	4%	-	-
Cefazolin	19	20	95%	12	20	60%	15	-	5	7	35%	1	7%	-	-
Gentamicin	30	34	88%	33	34	97%	31	1	2	1	3%	-	-	-	-
Amikacin	41	41	100%	41	42	98%	41	-	1	-	-	-	-	1	100%
Ceftazidime-avibactam	20	21	95%	20	21	95%	19	-	2	-	-	1	5%	-	
Overall	**752**	**771**	**98%**	**728**	**772**	**94%**	**595**	**23**	**154**	**37**	**5%**	**5**	**1%**	**2**	**1%**

Table 3. CA and EA
Yellow= values outside acceptance criteria

Results

Antimicrobial	EA	N	%	CA	N	%	S	I	R	mE	%	ME	%	VME	%
Ampicillin	21	21	100%	20	21	95%	5	1	15	1	5%	-	-	-	-
Ampicillin-sulbactam	41	42	98%	34	42	81%	25	6	11	8	19%	-	-	-	-
Meropenem-vaborbactam	52	52	100%	52	52	100%	52	-	-	-	-	-	-	-	-
Piperacillin-tazobactam	40	42	95%	41	42	98%	38	2	2	1	2%	-	-	-	-
Cefepime	52	54	96%	50	54	93%	38	1	15	4	7%	-	-	-	-
Cefuroxime	41	42	98%	41	42	98%	26	2	14	1	2%	-	-	-	-
Ceftazidime	49	50	98%	46	50	92%	33	2	15	3	6%	-	-	-	-
Aztreonam	51	51	100%	50	51	98%	36	1	14	1	2%	-	-	-	-
Meropenem	32	32	100%	32	32	100%	29	-	3	-	-	-	-	-	-
Tobramycin	50	50	100%	45	50	90%	44	2	4	5	10%	-	-	-	-
Tigecycline	49	50	98%	49	50	98%	49	1	-	1	2%	-	-	-	-
Ciprofloxacin	60	60	100%	57	60	95%	43	1	16	3	5%	-	-	-	-
Levofloxacin	61	61	100%	58	61	95%	43	4	14	3	5%	-	-	-	-
Trimethoprim-sulfamethoxazole	47	48	98%	47	48	98%	28	-	20	-	-	1	4%	-	-
Cefazolin	19	20	95%	13	20	65%	14	-	6	7	35%	-	-	-	-
Gentamicin	30	34	88%	33	34	97%	31	1	2	1	3%	-	-	-	-
Amikacin	42	42	100%	41	42	98%	41	-	1	-	-	-	-	1	100%
Ceftazidime-avibactam	20	21	95%	21	21	100%	19	-	2	-	-	-	-	-	-
Overall	**757**	**772**	**98%**	**730**	**772**	**95%**	**594**	**24**	**154**	**39**	**5%**	**1**	**0.2%**	**1**	**1%**

Table 4. CA and EA after discordant resolution
Yellow= values outside acceptance criteria

Antimicrobial	EA	N	%	CA	N	%	S	I	R	mE	%	ME	%	VME	%
Ampicillin	21	21	100%	20	21	95%	5	1	15	1	5%	-	-	-	-
Ampicillin-sulbactam	41	42	98%	34	42	81%	25	6	11	8	19%	-	-	-	-
Meropenem-vaborbactam	52	52	100%	52	52	100%	52	-	-	-	-	-	-	-	-
Piperacillin-tazobactam	40	42	95%	41	42	98%	38	2	2	1	2%	-	-	-	-
Cefepime	52	54	96%	50	52*	96%	38	1	13	2	4%	-	-	-	-
Cefuroxime	41	42	98%	41	42	98%	26	2	14	1	2%	-	-	-	-
Ceftazidime	49	50	98%	47	50	94%	33	2	15	3	6%	-	-	-	-
Aztreonam	51	51	100%	50	51	98%	36	1	14	1	2%	-	-	-	-
Meropenem	32	32	100%	32	32	100%	29	-	3	-	-	-	-	-	-
Tobramycin	49	49	100%	45	50	90%	44	2	4	4	8%	-	-	-	-
Tigecycline	49	50	98%	49	50	98%	49	1	-	1	2%	-	-	-	-
Ciprofloxacin	60	60	100%	57	60	95%	43	1	16	3	5%	-	-	-	-
Levofloxacin	60	60	100%	58	61	95%	43	4	14	3	5%	-	-	-	-
Trimethoprim-sulfamethoxazole	47	48	98%	47	48	98%	28	-	20	-	-	1	4%	-	-
Cefazolin	19	20	95%	13	20	65%	15	-	5	7	35%	1	7%	-	-
Gentamicin	30	34	88%	33	34	97%	31	1	2	1	3%	-	-	-	-
Amikacin	41	41	100%	41	42	98%	41	-	1	-	-	-	-	1	100%
Ceftazidime-avibactam	20	21	95%	21	21	100%	19	-	2	-	-	-	-	-	-
Overall	**754**	**769**	**98%**	**731**	**770**	**95%**	**595**	**24**	**151**	**36**	**5%**	**1**	**0.2%**	**1**	**1%**

Table 5. CA and EA after discordant resolution and CLSI 2025 breakpoint updates
Yellow= values outside acceptance criteria
*2 excluded

Conclusions

- Overall CA of 95% and EA of 98% was observed, demonstrating that the Q-linea ASTar® system can provide fast and reliable AST results within 6 h of blood culture positivity.
- While overall CAs and EAs were within the acceptable criteria, individual CAs were low for ampicillin-sulbactam and cefazolin, and individuals EAs for piperacillin-tazobactam and gentamicin were low.
- Discrepant analysis reduced the number of MEs and VMEs.
- Breakpoint updates did not significantly change the CA.
- The integration of rapid identification and rapid AST has the potential to significantly impact patient management by allowing for the quick optimization of therapy in patients with bloodstream infections.
- Further studies are necessary to fully understand the impact of rapid AST methods in BSI management.

Acknowledgements

- We thank Q-linea for providing the resources to conduct this study.