A Multisite Clinical Evaluation of the LifeScale AST System for Rapid Antimicrobial Susceptibility Testing of Gram-Negative Bacteria Direct from Blood Culture

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Abstract

Background:
Rapid antimicrobial susceptibility testing (AST) is critical for optimizing treatment outcomes and combating the rise of antimicrobial resistance. The LifeScale Gram-Negative Kit (LSGN) with the LifeScale AST system, developed by Affinity Biosensors (Santa Barbara, CA), is a multiplexed in vitro diagnostic test that utilizes a microfluidic sensor and resonant frequency to calculate organism concentration and mass distribution for quantitative AST. A multi-site clinical evaluation was conducted to assess the substantial equivalence of the LifeScale System's LSGN Panel for Gram-negative organisms compared to the CLSI reference broth microdilution method (BMD).

Methods:
The objective of the study was to establish the clinical performance of the LifeScale AST system with the LSGN panel in comparison to the FDA-recognized CLSI BMD for determining quantitative (MIC) AST results directly from Gram-negative positive blood cultures, including *Enterobacterales, Pseudomonas aeruginosa*, and *Acinetobacter spp*. Acceptable clinical performance for prospective, seeded clinical, challenge and reproducibility strains was assessed across the following parameters for 14 antimicrobial agents on the LSGN panel: essential agreement (EA), categorical agreement (CA), and the number and percent of categorical errors (minor, major, and very major errors). EA was calculated as the percentage of MIC results that fell within ± 1 doubling dilution of the reference result. CA was calculated as the percentage of the LifeScale interpretive results (S/SDD/I/R) that were identical to the interpretive categories of the BMD result. Reproducibility was determined from the total number (and percent) of results that fell within ± 1 doubling dilution of the modal MIC result, divided by the total number of results.

Results:
The overall EA and CA rates between the LifeScale AST system and the CLSI BMD for 5,762 *Enterobacterales* were 96.0% and 96.1%, for 680 *P. aeruginosa* were 94.6% and 91.2%, and for 362 *Acinetobacter spp*. were 95.6% and 97.0%, respectively. Overall reproducibility was 98.1%.

Conclusion:
The LifeScale AST system, using resonant frequency, offers advantages in speed, accuracy, and scalability when compared to conventional antimicrobial susceptibility testing methods. The high levels of EA and CA agreement rates from this multi-site evaluation position the LifeScale AST system as a gold standard in the rapid diagnostics landscape, with significant implications for improving patient care.

Introduction

Antimicrobial resistance (AMR) poses a critical threat to global health, with delays in appropriate antimicrobial therapy contributing to increased mortality, prolonged hospital stays, and rising healthcare costs. Traditional antimicrobial susceptibility testing (AST) methods, such as broth microdilution and disk diffusion, typically require 24-48 hours for results-time during which patients often receive empirical, and sometimes inappropriate, treatment.

Rapid AST technology such as Affinity Biosensors' LifeScale Rapid AST system, aims to significantly reduce the turnaround time, providing phenotypic susceptibility results within hours rather than days. This method, which includes microfluidics, rapidly assesses Gram-negative bacterial growth and antibiotic response, enabling faster determination of susceptibility profiles, (see Figure 1).

Enabling platforms like the LifeScale rapid AST exemplifies the shift toward faster, more precise diagnostic tools that are poised to become essential in both routine clinical care and the global response to antimicrobial resistance.

Introduction

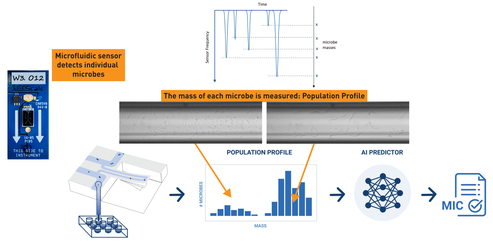

Figure 1, The LifeScale AST system utilizes population profiling to generate MIC results in under 5 hours

Methods

This study evaluated the clinical performance of the LifeScale AST system using the LSGN panel, (Figure 2), designed to deliver MIC results directly from Gram-negative positive blood cultures. Target organisms include *Enterobacterales, Pseudomonas aeruginosa,* and *Acinetobacter species.*

	1	2	3	4	5	6	7	8	9	10	11	12
A	MERO 0.125	FEP 0.5	AMI 4	ETP 0.125	LEVO 0.25	P/T 4	FAZ 0.25	AZT 1	TAZ 1	AMP 2	GEN 1	MEV 0.5
B	MERO 0.25	FEP 1	AMI 8	ETP 0.25	LEVO 0.5	P/T 8	FAZ 0.5	AZT 2	TAZ 2	AMP 4	GEN 2	MEV 1
C	MERO 0.5	FEP 2	AMI 16	ETP 0.5	LEVO 1	P/T 16	FAZ 1	AZT 4	TAZ 4	AMP 8	GEN 4	MEV 2
D	MERO 1	FEP 4	AMI 32	ETP 1	LEVO 2	P/T 32	FAZ 2	AZT 8	TAZ 8	AMP 16	GEN 8	MEV 4
E	MERO 2	FEP 8	AMI 64	ETP 2	LEVO 4	P/T 64	FAZ 4	AZT 16	TAZ 16	AMP 32	GEN 16	MEV 8
F	MERO 4	FEP 16	AMI 128	ETP 4	LEVO 8	P/T 128	FAZ 8	AZT 32	TAZ 32	AMP 64	GEN 32	MEV 16
G	MERO 8	FEP 32	AMI 256	ETP 8	LEVO 16	P/T 256	FAZ 16	AZT 64	TAZ 64	CZA 8	CZA 16	CZA 32
H	MERO 16	FEP 64	SXT 0.25	SXT 0.5	SXT 1	SXT 2	SXT 4	SXT 8	CZA 2	C/Z* 4	POS 0	POS 0

Antimicrobial		Range µg/ml	
		Min	Max
Amikacin	AMI	4	256
Ampicillin	AMP	2	64
Aztreonam	AZT	1	64
Cefazolin	FAZ	0.25	16
Cefepime	FEP	0.5	64
Ceftazidime	TAZ	1	64
Ceftazidime/Avibactam (+4)	CZA	2	32
Ertapenem	ETP	0.125	8
Gentamicin	GEN	1	32
Levofloxacin	LEVO	0.25	16
Meropenem	MERO	0.125	16
Meropenem/Vaborbactam	MEV	0.5	16
Piperacillin/Tazobactam (+4)	P/T	4	256
Trimethoprim/Sulfamethoxazole (1:9)	SXT	0.25	8

Figure 2. The LifeScale AST system LSGN Panel

The LifeScale AST results were compared against FDA-recognized CLSI broth microdilution (BMD) method, (Figure 3), which served as the reference method. Testing was conducted at 6 sites with a diverse strain set, including prospective clinical samples, seeded blood cultures, challenge and reproducibility strains. Performance was assessed for 14 antimicrobial agents;

- Amikacin
- Ampicillin
- Aztreonam
- Cefazolin
- Cefepime
- Ceftazidime
- Ceftazidime-Avibactam
- Ertapenem
- Gentamicin
- Levofloxacin
- Meropenem-Vaborbactam
- Piperacillin-Tazobactam
- Trimethoprim-Sulfamethoxazole

Performance of the LifeScale AST system was evaluated using three key metrics:

- Essential agreement (EA) which measured the percentage of MIC values within +/- 1 doubling dilution against the reference BMD method
- Categorical Agreement (CA), representing the proportion on interpretive results (S/SDD/I/R) that matched the BMD categories
- Frequency of categorical errors, including minor, major, and very major errors.
- Reproducibility was assessed by the consistency of MIC values across replicates, defined as the percentage of results within +/- 1 dilution of the LifeScale Modal MIC.

Methods

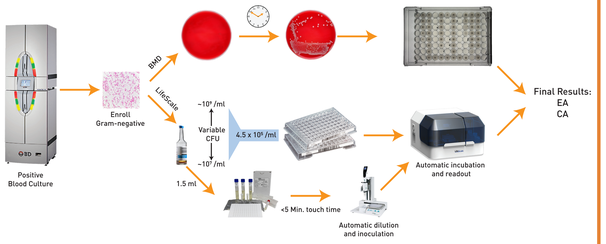

Figure 3, The LifeScale AST system workflow for direct from positive blood culture samples

Results

The LifeScale AST system demonstrated high overall agreement with the CLSI BMD reference method across all Gram-negative organisms. For *Enterobacterales* (n=5,762), the system achieved an EA of 96.0%, (Table 2), and a CA of 96.1%, (Table 3). Among *Pseudomonas aeruginosa* isolates (n=680), the EA was 94.6%, with a slightly lower CA of 91.2%. For *Acinetobacter spp*. (n=362), performance remained strong, with EA and CA rates of 95.6% and 97.0%, respectively. The overall reproducibility of the LifeScale AST system was 98.1%, confirming the system's consistency and reliability across multiple testing conditions, (Table 4).

These results support the LifeScale AST system as a robust and accurate method for rapid MIC-based susceptibility testing directly from positive blood cultures for a range of clinically relevant Gram-negative pathogens.

Table 1, Time to results by genus

Genus	TtR Slow Growing (HH:MM) (Additional Incubation Required)	TtR Workflow (HH:MM) (No Additional Incubation Required)	TtR Overall (HH:MM)
Acinetobacter	5:33	4:33	4:47
Escherichia	5:57	4:32	4:42
Klebsiella	5:31	4:46	4:51
Pseudomonas	5:41	4:55	5:18

Conclusions

The LifeScale AST system demonstrated excellent clinical performance across a broad spectrum of Gram-negative pathogens, showing high levels of agreement with the CLSI reference BMD method. With EA and CA rates consistently exceeding 94% across *Enterobacterales*, *Pseudomonas aeruginosa* and *Acinetobacter spp*., and an overall reproducibility of 98.1%, the system offers reliable and reproducible MIC-based susceptibility results direct from positive blood cultures.

Utilizing microfluidics and resonant frequency technology, LifeScale provides rapid, quantitative AST results within 4.5 hours significantly reducing the time to targeted therapy. This speed advantage, coupled with robust accuracy, positions LifeScale as the leading solution in the rapidly evolving field of infectious disease.

These findings support the integration of the LifeScale AST system into clinical workflows, where its impact on earlier therapeutic decision-making, antimicrobial stewardship, and improved patient outcomes could be substantial. The results of this multi-site evaluation confirm that the LifeScale AST system delivers exceptional speed, accuracy, and reproducibility, making it the leading solution in the field of rapid antimicrobial susceptibility testing.

Results

Table 2, Overall essential agreement

Organism	Essential Agreement (%)													
	AMI	AMP	AZT	FAZ	FEP	TAZ	CZA	ETP	GEN	LEVO	MERO	MEV	P/T	SXT
Enterobacterales	97.3%	100%	95.2%	97.4%	92.6%	97.2%	99.0%	94.8%	98.8%	98.2%	91.6%	95.0%	90.8%	99.1%
Pseudomonas aeruginosa	98.3%	-	-	-	93.1%	92.2%	-	-	94.9%	96.0%	96.6%	-	94.1%	-
Acinetobacter baumannii	100%	-	-	-	-	94.9%	-	-	-	-	96.2%	-	-	-

Table 3, Overall categorical agreement

Organism	Categorical Agreement (%)													
	AMI	AMP	AZT	FAZ	FEP	TAZ	CZA	ETP	GEN	LEVO	MERO	MEV	P/T	SXT
Enterobacterales	95.8%	100%	96.7%	89.6%	95.7%	97.8%	99.0%	95.6%	97.7%	96.6%	96.7%	94.6%	92.1%	99.1%
Pseudomonas aeruginosa	94.9%	-	-	-	84.2%	94.0%	-	-	93.2%	88.1%	89.8%	-	93.5%	-
Acinetobacter baumannii	97.4%	-	-	-	-	98.3%	-	-	-	-	97.4%	-	-	-

Table 4, Reproducibility by antibiotic

Antimicrobial	Best Case No. Within 1 +/- Dil/ Total Tests (%)	Worst Case No. Within 1 +/- Dil/ Total Tests (%)
Ampicillin	268/269 = 99.6%	250/269 = 92.9%
Amikacin	468/481 = 97.3%	450/481 = 93.6%
Aztreonam	290/294 = 98.6%	263/294 = 89.5%
Cefazolin	321/324 = 99.1%	321/324 = 99.1%
Cefepime	504/509 = 99.0%	459/509 = 90.2%
Ceftazidime	264/265 = 99.6%	244/265 = 92.1%
Ceftazidime-avibactam	345/350 = 98.6%	339/350= 96.9%
Ertapenem	291/296 = 98.3%	271/296 = 91.6%
Gentamicin	503/509 = 98.8%	466/509 = 91.6%
Levofloxacin	373/373 = 100%	361/373 = 96.8%
Meropenem	508/534 = 95.1%	477/534 = 89.3%
Meropenem-vaborbactam	274/287 = 95.5%	261/287 = 90.9%
Piperacillin-tazobactam	555/566 = 98.1%	521/566 = 92.0%
Trimethoprim-sulfamethoxazole	255/264 = 96.6%	243/264 = 92.0%

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