Accelerate Pheno System (AXDX) performance during a randomized clinical trial evaluating rapid identification and antimicrobial susceptibility testing for Gram negative bacteremia (RAPIDS-GN)

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Abstract

Background: The RAPIDS-GN trial is an ongoing prospective randomized controlled trial comparing clinical outcomes of patients with Gram negative bacteremia who have blood culture testing using the Accelerate Pheno System (AXDX) vs. standard of care (SOC) culture and antimicrobial susceptibility testing (AST) in combination with antimicrobial stewardship. We analyze AXDX performance compared to SOC in subjects enrolled to date.

Methods: In RAPIDS-GN, subjects with positive blood cultures demonstrating Gram negative bacilli on Gram stain are randomized to receive either AXDX plus SOC testing, or SOC testing alone. Subjects who were enrolled between 10/9/17-1/2/18, randomized to both AXDX and SOC testing and had microbiology data available were included in this analysis. ID and AST discrepancies were quantified. AST discrepancies were categorized as very major, major, or minor errors.

Results: Among 46 isolates identified by SOC, 37 (80%) were organisms present on the AXDX panel, and 9 (20%) were off-panel organisms. Among 37 isolates present on the AXDX panel, 34 (92%) were identified by both AXDX and SOC, and 3 (8%) were detected by SOC but not AXDX (Table 1). In 4 polymicrobial cultures with >1 organism identified by SOC, AXDX identified only 1 organism per culture. Of 369 susceptibility tests performed using both AXDX and SOC, there were 24 (6.5%) minor errors and 1 (0.3%) major error (Table 2). The AXDX AST was less susceptible than SOC AST in 24/25 (96%) AST errors.

Conclusion: In preliminary analysis of participants enrolled in the RAPIDS-GN trial, 74% of Gram negative organisms isolated from blood cultures were detected using AXDX. Among only organisms present on the panel, AXDX identified >90% of organisms that were identified by SOC, with few minor or major errors in AST.

Background

- The Accelerate PhenoTest BC Kit (AXDX) is an FDA approved platform that performs rapid bacterial identification within 1.5 hours and AST within 7 hours directly from positive blood cultures.
- The RAPIDS-GN study is an ongoing 2 site prospective randomized controlled trial of patients with confirmed Gram-negative bacillus bacteremia.
- The **objective** of RAPIDS-GN is to determine the impact of rapid bacterial identification and phenotypic antimicrobial susceptibility testing (AST) on antimicrobial usage and clinical outcomes among patients with Gram negative bacteremia.
- We present preliminary analysis of AXDX performance compared to standard of care (SOC) methods for culture and AST in subjects enrolled to date.

Figure 1. Study Design of RAPIDS GN trial

Patients with Gram-negative bacilli in blood culture bottle

Randomization

SOC testing + Antimicrobial Stewardship
- Gram stain called to service
- Standard subculture and AST
- Antimicrobial stewardship

SOC + AXDX+ Antimicrobial Stewardship
- Gram stain called to service
- Standard subculture and AST
- Rapid test + lab call
- Antimicrobial stewardship

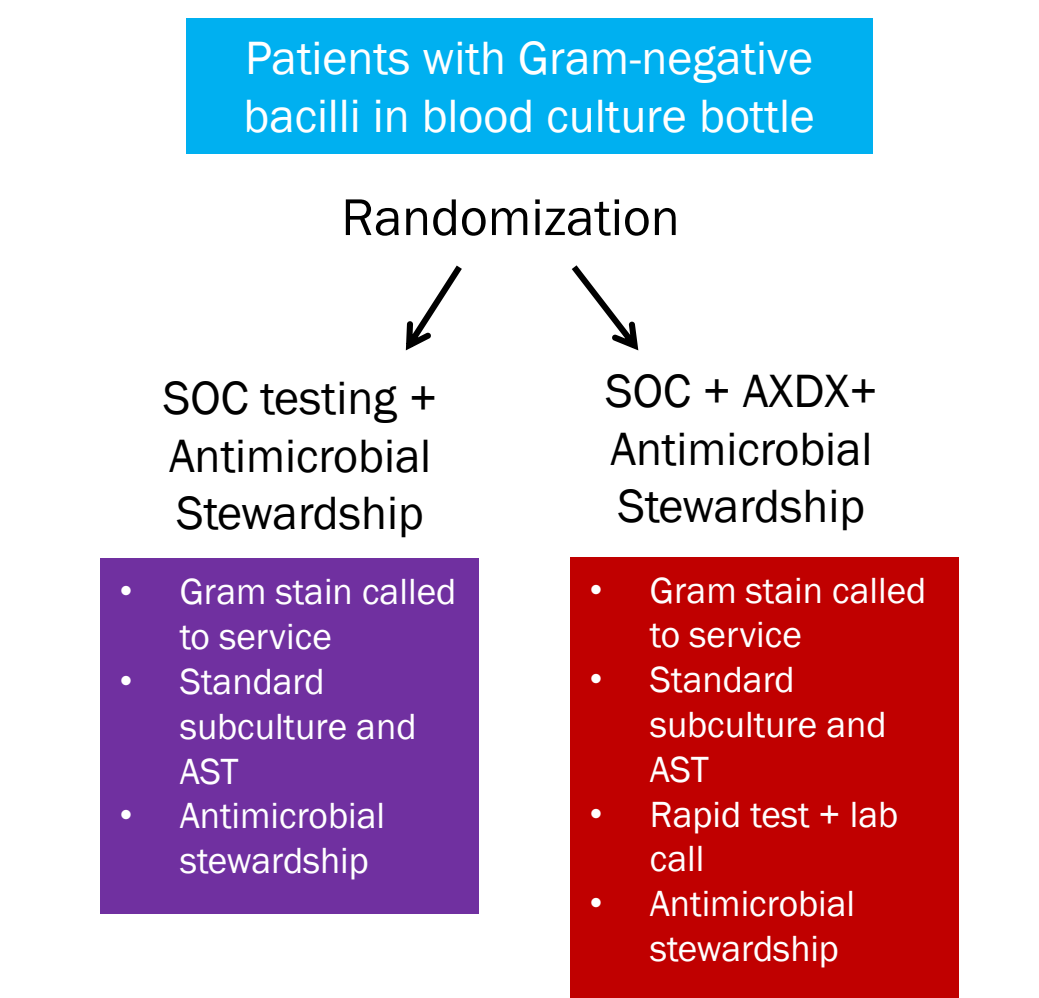SOC, standard of care; AXDX, Accelerate Pheno testing; AST, antimicrobial susceptibility testing

Methods

- Subjects with positive blood cultures demonstrating Gram negative bacilli on Gram stain are randomized to receive either AXDX plus SOC testing, or SOC testing alone (**Figure 1**).
- Subjects enrolled between 10/9/17-5/2/18, randomized to both AXDX and SOC testing, and with microbiology data available were included in this analysis.
- ID and AST discrepancies were quantified and updated from originally submitted abstract.
- AST discrepancies categorized as very major (susceptible by AXDX, resistant by SOC), major (resistant by AXDX, susceptible by SOC), or minor errors (intermediate by one method, susceptible or resistant by the other).
- When multiple morphotypes of a species were present, the culture was considered polymicrobial but only the more resistant morphotype was included in analyses.

Table 1. Characteristics of cultures and isolates

Characteristic	No (%)
Monomicrobial cultures	115/123 (94%)
Polymicrobial cultures	8/123 (6%)
Isolates on AXDX Panel	114/127 (90%)
Isolates not on AXDX Panel	13/127 (10%)

*Due to polymicrobial cultures, there are more isolates than cultures.
**Cultures with multiple morphotypes of a species were considered polymicrobial but were counted as a single isolate in analysis.

Results

- 131 subjects randomized to AXDX arm; 123 subjects with available data
- 90% of isolates were targets on the AXDX panel (**Table 1**)
- *E. coli* was the most commonly identified organism (45% of all isolates)
- Among on-panel organisms (**Table 2**)
  - AXDX identified 89%
  - AXDX did not identify 11%
- AST discrepancies between SOC and AXDX were rare (**Table 3**)
  - minor errors (6%)
  - major errors (1%)
  - very major errors (0%)
- The antibiotic accounting for most AST discrepancies was ampicillin-sulbactam (32% of minor and 36% of major errors).
- In 59/68 (87%) minor and major errors, AXDX AST result was less susceptible than SOC (**Table 4**).

Table 2. Organism identification, SOC vs. AXDX.

Species	No. identified by SOC	No. (%) identified by both SOC and AXDX	No. (%) Identified by SOC but not AXDX*
All isolates	127	101 (79)	26 (21)
On-panel isolates	114	101 (89)	13 (11)
E. coli	57	51 (89)	6 (11)
Enterobacter spp.	7	5 (71)	2 (29)
Klebsiella spp.	31	28 (90)	3 (10)
Pseudomonas spp.	15	13 (87)	2 (13)
Serratia spp.	3	3 (100)	0
Proteus spp.	1	1 (100)	0

SOC, standard of care; AXDX, Accelerate Pheno System; *Polymicrobial cultures accounted for 6/13 (46%) cultures when some organisms were identified by both SOC and AXDX, but there was at least 1 AXDX identification error.

Table 3. AST discrepancies, SOC vs. AXDX

Antibiotic	No. of tests SOC and AXDX	Minor errors No. (%)	Major errors No. (%)
All	998	57 (6)	11 (1)
Amikacin	90	1 (1)	0
Ampicillin-sulbactam	58	18 (31)	4 (7)
Aztreonam	67	1 (2)	1 (2)
Cefepime	90	4 (4)	1 (1)
Ceftazidime	84	9 (11)	0
Ceftriaxone	79	2 (3)	0
Ciprofloxacin	89	0	0
Ertapenem	79	0	0
Gentamicin	91	1 (1)	1 (1)
Meropenem	89	6 (7)	2 (2)
Piperacillin-tazobactam	91	12 (13)	2 (2)
Tobramycin	91	3 (3)	0

Row % is shown. SOC, standard of care; AXDX, Accelerate Pheno System; AST, antimicrobial susceptibility testing. No very major errors occurred.

Table 4. Details of 11 major AST discrepancies, SOC vs. AXDX.

Organism (# of isolates)	Antibiotic	SOC AST	AXDX AST
Pseudomonas (1)	Gentamicin	S	R
	Meropenem	S	R
Enterobacter (1)	Aztreonam	S	R
	Cefepime	S	R
E. coli (2)	Piperacillin-tazobactam	S	R
E. coli (2)	Ampicillin-sulbactam	S	R
E. coli (1)	Meropenem	S	R
Klebsiella (2)	Ampicillin-sulbactam	S	R

SOC, standard of care; AXDX, Accelerate Pheno System; AST, antimicrobial susceptibility testing. S, susceptible; R, resistant

Conclusions

In preliminary analysis of participants enrolled in the RAPIDS-GN trial:

- 79% of Gram negative organisms isolated from blood cultures were detected using AXDX.
- Among only organisms present on the panel, AXDX identified nearly 90% of organisms that were identified by SOC.
- There were few minor or major errors in AST.

Disclosures

Accelerate Diagnostics provided instruments and partial support for reagents but had no role in study design or implementation of the trial.

Contact

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