Evaluation and potential clinical impact of a rapid AST method direct from Gram-negative blood cultures

Noah Henry, Paula Binsol, Katelyn Teckenbrock, Monish Sheth, Sangeetha Ranganath, Tiffany LaDow, Ryan Beaver, Lauren Sisco, John Midturi and Manohar Mutnal

Department of Pathology and Laboratory Medicine, Baylor Scott & White Medical Center, Texas, USA.

Introduction

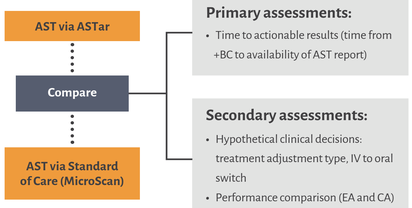
Patients with bloodstream infections or sepsis need appropriate antimicrobial treatments to improve outcomes and reduce mortality. Timely Antimicrobial Susceptibility Testing (AST) is crucial.

In this retrospective non-interventional study, we evaluated the performance of ASTar, a fully automated rapid AST system from Q-linea[1], and its hypothetical clinical impact when treating patients with Bloodstream Infections (BSIs), comparing it to our routine AST methods.

Conclusion

- ASTar can save over 38 hrs from +BC to AST result as compared to our standard of care (SoC) method (MicroScan)
- ASTar performance aligns with traditional BMD – overall EA and CA >90%
- ASTar can potentially impact clinical decisions and support optimized targeted therapy sooner

Methods



- We aim for target enrolment of 100 positive blood cultures from patients admitted to the hospital with a monobacterial, Gram-negative BSI: 34 samples tested between March-June 2024 were included in this interim analysis
- AST via ASTar run in parallel to our SoC method (MicroScan), and performance and hypothetical clinical impact compared between methods

References

1. Göransson, J *et al.* "Performance of a System for Rapid Phenotypic Antimicrobial Susceptibility Testing of Gram-Negative Bacteria Directly from Positive Blood Culture Bottles." Journal of clinical microbiology vol. 61,3 (2023): e0152522. doi:10.1128/jcm.01525-22
2. ISPOR. https://www.ispor.org/heor-resources/about-heor, 2024
3. FDA. https://www.fda.gov/drugs/development-resources/antibacterial-susceptibility-test-interpretive-criteria.

Results

ASTar can expedite the clinical workflow

We calculated the median time for all critical clinical and laboratory events for patient data used in this interim analysis, as shown in Figure 1.

Hypothetically, ASTar has the potential to deliver actionable results to the treating clinician faster than our SoC MicroScan method (12.1 h from positive blood culture versus 50.7 h) and could expedite the clinical workflow. From sample load, ASTar takes approx. six hours to complete a run.

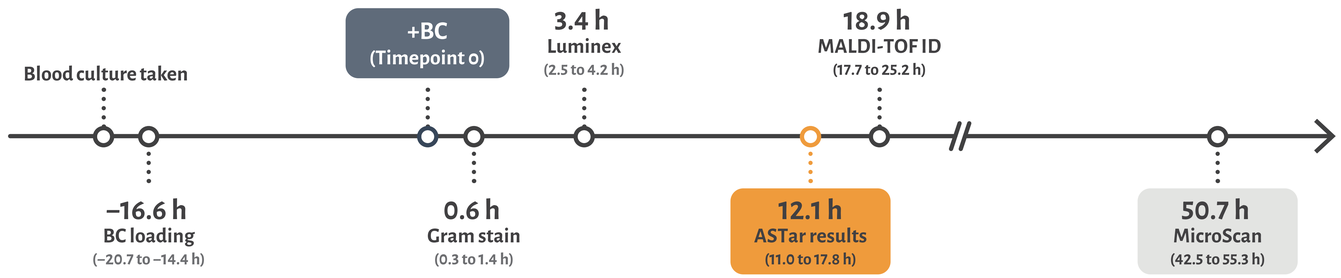


Figure 1. Median time to critical events. Interquartile ranges (IQR) in brackets.

+BC = Postive Blood Culture Bottle

ASTar delivers actionable results >38 hours faster than SoC

AST of patient samples was run in parallel using ASTar and MicroScan. The median time to results (TTR) was compared between each method and paired patient samples.

Median time from +BC to ASTar results was 12.1 h (7.2 h –22.0 h). Median time from +BC to MicroScan results was 50.7 h (30.0–89.0 h). The overall time difference between methods was 38.6 h. (Figure 2).

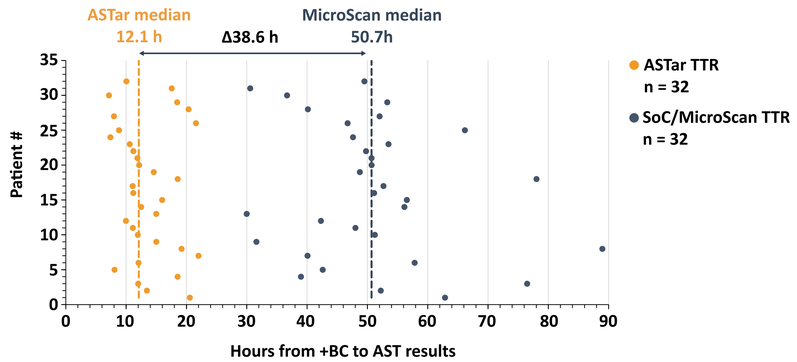


Figure 2. Paired patient samples from ASTar and MicroScan AST. Median time from +BC to ASt results.

ASTar can potentially impact clinical decisions and support optimized targeted therapy

For the 34 patient samples included in this interim analysis that had complete case reports, we investigated how timely ASTar results could have potentially impacted treatment adjustment and clinical decisions, as shown in Figure 3.

In 56% of patients, we see that ASTar could have prompted earlier de-escalation of empiric therapies. In the remaining 44% of cases, ASTar could have guided other types of treatment adjustment, dependent on the individual cases.

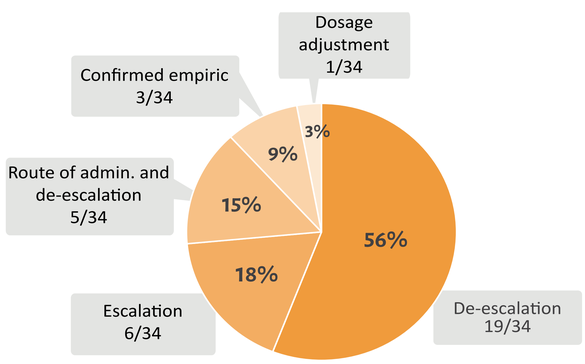


Figure 3. Overview of the potential clinical impact and type of antibiotic change that ASTar can drive.

ASTar performed at 98% total EA and 94% total CA

MIC data was interpreted and assessed for all tested antibiotics using FDA STIC breakpoints[3]. A discrepancy resolution has not yet been performed.

ASTar maintained a high agreement with our reference SoC method (MicroScan), as assessed by an overall EA of 98%, CA of 94%, VMD rate of 2.9%, and MD rate of 0.8% (Table 1 and 2).

Table 1. Overall performance data. Essential Agreement (EA), Categorical Agreement (CA), Very Major Discrepancy (VMD), Major Discrepancy (MD).

ASTar vs. MicroScan			
EA #/tot (%)	CA #/tot (%)	VMD #/tot (%)	MD #/tot (%)
424/433 (98%)	407/433 (94%)	*2/68 (2.9%)	3/354 (0.8%)

*1/68 VMDs when using FDA STIC (2024) version.

Table 2. Performance data for all antibiotics used in the study. FDA STIC (2023) breakpoints.

Antimicrobial agent	ASTar vs. MicroScan	
	EA #/tot (%)	CA #/tot (%)
Ampicillin	25/25 (100%)	25/25 (100%)
Ampicillin-sulbactam	33/33 (100%)	29/33 (88%)
Cefazolin	31/33 (94%)	22/33 (67%)
Cefepime	32/34 (94%)	33/34 (97%)
Ceftazidime	33/34 (97%)	33/34 (97%)
Ceftazidime-avibactam	1/1 (100%)	1/1 (100%)
Ceftriaxone	34/34 (100%)	34/34 (100%)
Cefuroxime	32/33 (97%)	30/33 (100%)
Ertapenem	1/1 (100%)	1/1 (100%)
Gentamicin	33/34 (97%)	34/34 (100%)
Levofloxacin	34/34 (100%)	32/34 (94%)
Meropenem	34/34 (100%)	34/34 (100%)
Meropenem-vaborbactam	1/1 (100%)	1/1 (100%)
Piperacillin-tazobactam	33/34 (97%)	32/34 (94%)
Tobramycin	34/34 (100%)	32/34 (94%)
Trimethoprim-sulfamethoxazole	33/34 (97%)	34/34 (100%)

Note: data from this study was generated on an ASTar BC G- IUO panel and not the FDA-cleared product