

Advantages of the AS*T*ar System

Broad antimicrobial panel and true MIC results for early and adequate treatment of bloodstream infections

Current standards of care for patients with a Gram-negative bloodstream infection are not always optimal. This is mostly due to the time lag between blood sampling, blood culture positivity, and antimicrobial susceptibility test (AST) results. The AS*T*ar[®] Instrument and BC G– Kit covers the broadest Gram-negative antimicrobial panel and range of dilutions to date. With this ideal testing capacity, AS*T*ar abolishes the need for extrapolated values, allowing all required antimicrobial dilutions to be tested simultaneously. Major advantages of the AS*T*ar Instrument and BC G– Kit for the lab, clinicians, and patients are a boosted workflow efficiency, less hands-on labor, faster AST results, and early start of adequate antimicrobial treatment.

Introduction

To cope with growing antimicrobial resistance, rapid diagnostic methods are needed. In regions with a high incidence of resistance, several antimicrobials already require to be used at relatively high concentrations, sometimes even at breakpoint. This emphasizes the continuing need for antimicrobial stewardship programs, and for the development of rapid techniques for the identification of pathogens (rapid ID) and rapid antimicrobial susceptibility testing (AST) technology (1-3). In the current standard of care, AST for bloodstream infections is completed at the earliest 48 hours after blood draw, although workflows may differ between laboratories. Due to this delay, clinicians are forced to rely on empiric therapy during the first days of treatment. This blind and potentially inappropriate antimicrobial therapy not only drives the development of resistance, but also prolongs patient hospitalization and increases mortality risk (4,5).

AS*T*ar – Rapid AST Results Directly From Clinical Samples

AS*T*ar is a new, fully automated system for rapid AST. The proprietary AST technology is based on broth microdilution (BMD) optimized for short time-to-result, delivering phenotypic AST with true minimum inhibitory concentration (MIC) results within approximately six hours. The first application is focused on Gram-negative bloodstream infections, to provide rapid AST results directly from positive blood cultures.

The AS*T* Disc

The AS*T* Disc contains more than 330 culturing chambers prefilled with antimicrobials in various concentrations used for AST, chambers without antimicrobials used as controls, and chambers used to determine the concentration in the purified sample. The Disc is labeled with a unique barcode for identification, and linking to each respective sample preparation Cartridge and patient. The antimicrobial panel for AST analysis of Gram-negative bacteria includes testing capacity for both non-fastidious and fastidious pathogens, directly from positive blood cultures. The availability of a broad panel with “old” and “novel” antibiotics offers multiple therapeutic options, while preserving the efficacy of new molecules. The optimal design allows for Disc storage at room temperature.



Figure 1. The AS*T*ar System covers the broadest Gram-negative antimicrobial panel and range of dilutions to date, in a user-friendly and fully automated rapid AST system. The instrument is designed to deliver AST testing from positive blood cultures in ~6 hours.

ASTar BCG-		Reportable range																Dilutions	
Non-fastidious		(mg/L)	0.008	0.015	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	
Amikacin	0.5	128																	9
Gentamicin	0.25	32																	8
Tobramycin	0.06	32																	10
Ertapenem	0.015	16																	11
Meropenem	0.06	64																	11
Cefazolin	0.25	16																	7
Cefepime	0.25	64																	9
Cefotaxime	0.015	128																	14
Cefoxitin (screen)	1	64																	7
Ceftazidime	0.25	64																	9
Ceftazidime-avibactam ¹	0.125	32																	9
Ceftolozane-tazobactam ²	0.125	32																	9
Ceftriaxone	0.015	128																	14
Cefuroxime	1	64																	7
Ciprofloxacin	0.06	8																	8
Levofloxacin	0.125	16																	8
Trimethoprim-sulfamethoxazole ³	0.06	8																	8
Aztreonam	0.25	64																	9
Amoxicillin-clavulanic acid ⁴	1	32																	6
Ampicillin	1	64																	7
Piperacillin-tazobactam ²	0.25	256																	11
Colistin	0.25	8																	6
Tigecycline	0.03	16																	10
Fastidious																			
Meropenem	0.015	8																	10
Cefotaxime	0.015	2																	8
Ceftriaxone	0.03	2																	7
Levofloxacin	0.03	8																	9
Amoxicillin-clavulanic acid ⁴	0.5	32																	7
Ampicillin	0.03	4																	8

¹ For susceptibility testing purposes, the concentration of avibactam is fixed at 4 mg/L

² For susceptibility testing purposes, the concentration of tazobactam is fixed at 4 mg/L

³ Trimethoprim:sulfamethoxazole in the ratio 1:19

⁴ For susceptibility testing purposes, the concentration of clavulanic acid is fixed at 2 mg/L

The Advantages of a Broad Panel and Ideal Disc Space

In optimising the care for patients with a bloodstream infection, it is particularly advantageous to have rapid access to precise Minimum Inhibitory Concentration (MIC) results. Early initiation of optimal therapy reduces the risk of disease progression and improves patient outcomes (1). In addition, the risks of side effects from prolonged broad-spectrum antibiotic exposure are reduced. With the aid of early optimal treatment, there is a realistic potential to reduce ICU length of stay, therefore generating cost savings.

According to key opinion leaders (KOLs), clinical microbiology laboratories, as well as the EUCAST committee, there is a distinct need for a broad range of antimicrobial dilutions for use in AST. The importance of a broad range of antimicrobial dilutions was emphasized as greater than the number of different antimicrobials. With the ASTar System, there is no need to compromise between these two, as ASTar fulfils both requirements. ASTar provides a broad range of antimicrobial dilutions that are measured simultaneously, whilst also featuring a testing capacity from very low to very high MIC values. The 23 antimicrobial compounds are for treatment against non-fastidious organisms, and six of these can treat infections caused by fastidious organisms. The space on the ASTar BCG- Disc allows for testing of 6-14 two-fold dilutions per antimicrobial in one run. The Disc design

is therefore ideal for use in European clinical microbiology settings, as the need for any extrapolated values is abolished, and results represent true MIC values. The current panel consists of 256 dilution points. However, there is room to add additional types of antimicrobials in the future, without the need to remove any of the existing antimicrobials present on the panel. The MIC-driven optimal dosing regimen can support the prevention of antimicrobial overdosing and underdosing.



Figure 2. The Disc during AST reading. The unique proprietary technology allows automated time-lapse imaging of bacterial population growth in wells containing different concentrations of antimicrobial agents.

Conclusion

ASTar can be started independently of ID, which is entered before, during or after the AST run to create the final MIC report. AST is initiated directly from a positive blood culture, which means that the total time to adequate antimicrobial treatment is shortened by approximately 25 hours compared with current practice. The fully-automated AST solution reduces hands-on time to a few minutes and improves data quality. Thanks to the novel disc design supporting a comprehensive AST panel, the simultaneous measurement of a broad range antimicrobial dilutions for MIC determination is possible, supporting potential reductions in the the need for follow up testing.

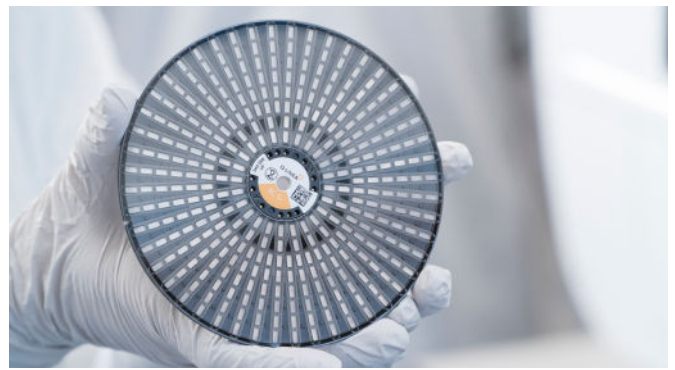


Figure 3. Optimized therapy in one go. The extensive Antimicrobial Susceptibility Testing capabilities of the AST Disc delivers clinically actionable results in a single run.

References

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Q: In your opinion, what are the advantages for a microbiologist of having a broad antibiotic panel with extended ranges? Could you please provide some clinical examples in support of your statement?

A: When performing AST, accurate measurement of MIC values is essential for correct categorization of antimicrobial susceptibility of bacterial isolates, which drives the selection of regimens and dosages for definitive antimicrobial therapy. When dealing with multidrug-resistant isolates, it is also important to test a broad panel of antibiotics to identify the few available options.

Systems that extrapolate MIC values from few data points may suffer from low accuracy, especially with multidrug-resistant isolates and drugs that are crucial to their treatment (e. g. carbapenems, polymyxins). For this reason, the availability of automated systems that can rapidly and accurately measure MICs for a broad antibiotic panel would be of great clinical interest.

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