Q-LINEA

Advantages of the ASTar 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 ASTar® Instrument and BC G– Kit covers the broadest Gram-negative antimicrobial panel and range of dilutions to date. With this ideal testing capacity, ASTar abolishes the need for extrapolated values, allowing all required antimicrobial dilutions to be tested simultaneously. Major advantages of the ASTar 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 con-tinuing need for antimicrobial stewardship programs, and for the development of rapid techniques for the identification of pathogens (rapid ID) and rapid anti-microbial susceptibility testing (AST) technology (1-3). In the current standard of care, AST for bloodstream infec-tions 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).

ASTar – rapid AST results directly from clinical samples

ASTar 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 AST Disc

The AST 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.

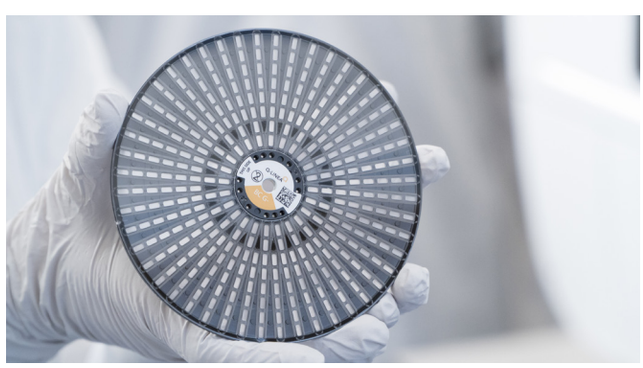
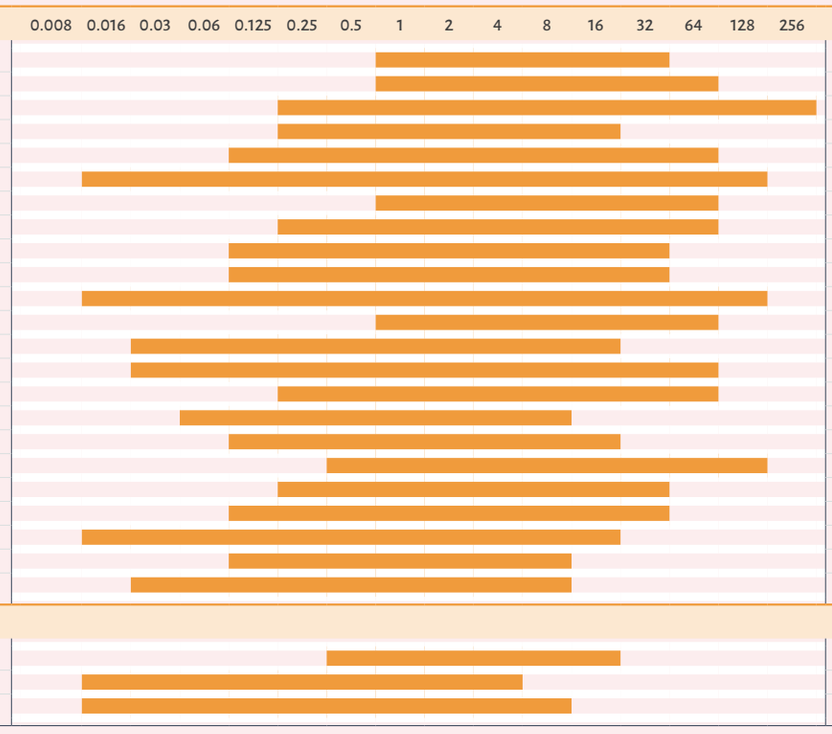


Figure 1. Optimized therapy in one go. The extensive Antimicrobial Susceptibility Testing capabilities of the AST Disc delivers clinically actionable results in a single run. The unique proprietary technology allows automated time-lapse imaging of bacterial population growth in wells containing different concentrations of antimicrobial agents.

ASTar BC G–	Reportable range		Dilutions
Non-fastidious	(mg/mL)		
Amoxicillin-clavulanic acid[1]	1	32	6
Ampicillin	1	64	7
Piperacillin-tazobactam[2]	0.25	256	11
Cefazolin	0.25	16	7
Cefepime	0.125	64	10
Cefotaxime	0.016	128	14
Cefoxitin (screen)	1	64	7
Ceftazidime	0.25	64	9
Ceftazidime-avibactam[3]	0.125	32	9
Ceftolozane-tazobactam[2]	0.125	32	9
Ceftriaxone	0.016	128	14
Cefuroxime	1	64	7
Ertapenem	0.03	16	10
Meropenem	0.03	64	12
Aztreonam	0.25	64	9
Ciprofloxacin	0.06	8	8
Levofloxacin	0.125	16	8
Amikacin	0.5	128	9
Gentamicin	0.25	32	8
Tobramycin	0.125	32	9
Tigecycline	0.016	16	11
Colistin	0.125	8	7
Trimethoprim-sulfamethoxazole[4]	0.03	8	9
Fastidious			
Amoxicillin-clavulanic acid*	0.5	16	6
Ampicillin*	0.016	4	9
Levofloxacin*	0.016	8	10



* fastidious antimicrobials

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

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

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

[4] Trimethoprim:sulfamethoxazole in the ratio 1:19

The advantages of a broad panel and ideal Disc space

In optimizing 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 adequate therapy reduces the risk of disease progression, and improves patient out-come (1). In 'addition, the risks of side effects from prolonged broad-spectrum antibiotic exposure are reduced. More-over, there is a realistic potential to reduce ICU-length of stay, thus generating cost savings. From several clinical microbiology labs, as well as the EUCAST committee, the distinct need for a broad range of antimicrobial dilutions was emphasized over the number of different antimicrobials. With the ASTar System there is no need to compromise between these two, as it provides a broad range in antimicrobial dilutions to be measured simultaneously, while featuring a testing capacity from very low to very high MIC values for 23 different antimicrobial compounds against non-fastidious organisms, and three against a fastidious organism. The space on the ASTar BC G– Disc allows for testing of 6-14 two-fold dilutions per antimicrobial in one run. The Disc design is thus ideal for the use in European clinical microbiology settings, as the need for any extrapola-ted values is abolished, and results represent true MIC values. In addition, with the current panel (235 dilution points) there is room to add on more types of anti-microbials without the need to take any of the existing panel away. The MIC-driven selection of the optimal dosing regimen in an MIC-driven dosing regimen can support preventing antimicrobial overdosing and underdosing.

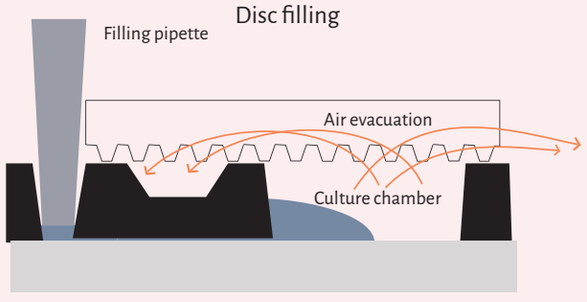


Figure 2. A schematic close up cross section of the Disc, illustrating the process of filling the culture chamber wells with concentration-controlled bacterial inoculate.

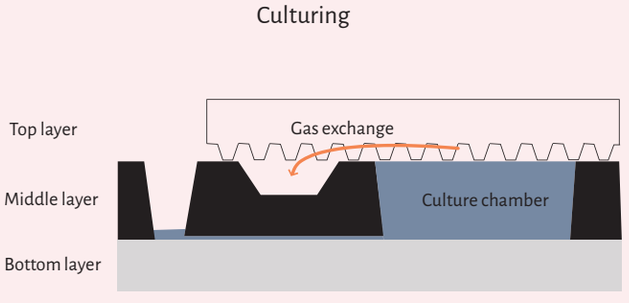


Figure 3. A schematic close-up cross section of the Disc, illustrating gas exchange during bacterial culture.

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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.

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 4. The ASTar 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.

References
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4. *Huang et al. Clin Infect Dis. 2013;57(9):1237-45*
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