Evaluation of Q-linea ASTar® System for rapid-antimicrobial susceptibility testing (rAST) of positive blood cultures: Comparison of susceptibility results; ASTar System, In-house Multipoint breakpoint and Sensititre®.

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BACKGROUND

The Q-linea ASTar System is a fully automated instrument for rAST that provides robust and consistent inoculum preparation for AST with high-speed time-lapse microscopy imaging of pathogen in broth microdilution to determine minimal inhibitory concentration, MIC. The streamlined workflow consisting of 3 consumables (figure 1) delivers a route to significantly speed up AST, offering the potential to positively impact patient outcomes associated with bacterial bloodstream infections (BSI).

We aim to determine that the ASTar panel covers >95% of the most common BSI and that the antibiogram results from ASTar are >95% in essential agreement compared to the gold-standard equivalent broth microdilution based Sensititre System and assessment of concordant category interpretation with Sheffield Teaching Hospitals 'in-house' multipoint method – breakpoint agar incorporation.

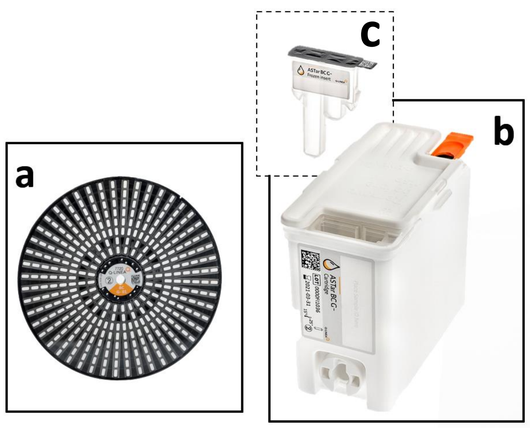


Figure 1.
a) AST disc: Design with ample space for 23 antimicrobials with 6-14 two-fold dilutions, covering 235 dilutions.

b) Sample cartridge: Generates a clean, controlled inoculum, dilution and growth medium adaptation.

c) Frozen insert: Inserted into cartridge to deliver reagents for sample preparation and fastidious organisms

MATERIALS

To collect data from at least 80 positive blood cultures where Gram negative bacilli were seen on the initial Gram film, including; time taken to process specimen for ASTar system, time to result (TTR), time to reportable susceptibility results available, antibiogram (ASTar system, multipoint and Sensititre system) and organism identification by MALDI TOF MS. Sensititre plates were processed according to manufacturer's instructions. Multipoint susceptibility results were produced according to laboratory SOP. At STH, direct sensitivity is performed on positive blood cultures where Gram negative bacilli are encountered and an antibiogram is available within 24 hours of the blood culture becoming positive. Sensititre plates and ASTar system testing were processed according to manufacturers instructions.

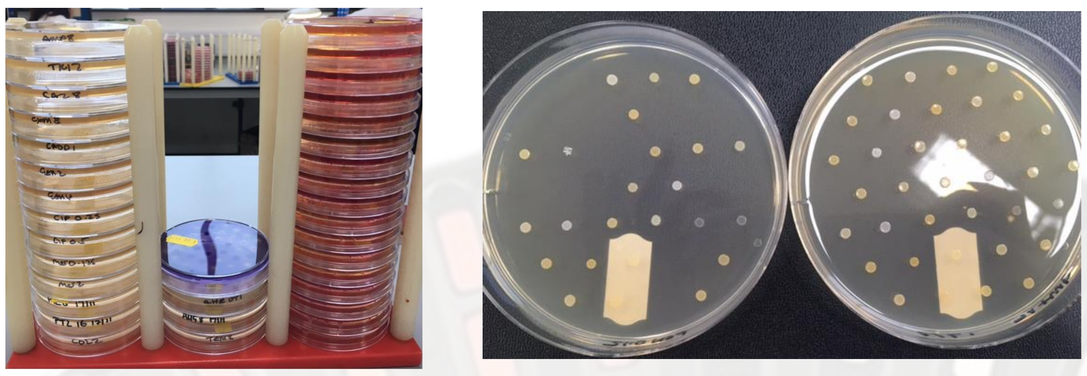
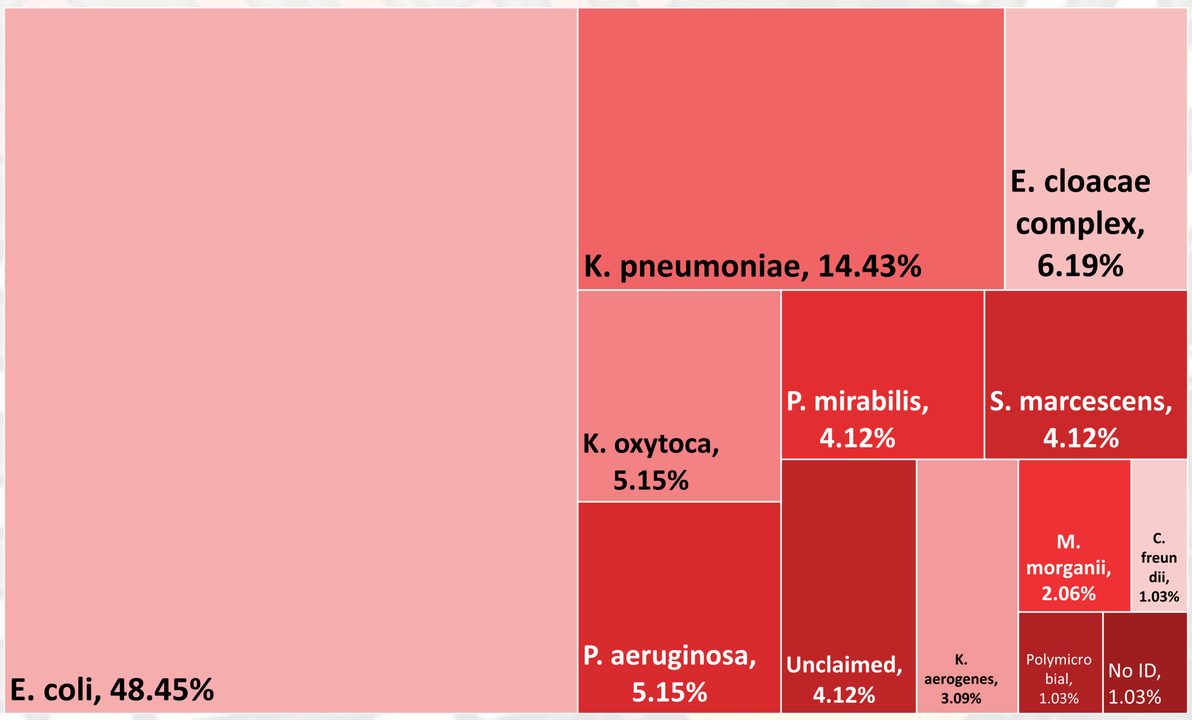


Figure 2. Multipoint antibiotic agar incorporation. A maximum of 36 isolates can be tested per plate, each breakpoint is set by EUCAST guidelines, result interpretation is qualitative.

RESULTS

Figure 3. Percentage of study isolates identified by MALDI TOF MS.



Of species identified in the study, 95.3% were covered by the ASTar panel, with only 3 anaerobes and a *Stenotrophomonas maltophilia not being covered*. Figure 3 shows the range of organisms tested during the evaluation. Operator 'hands on time' averaged <4 minutes.

Table 1 highlights antibiotic concordance ASTar system vs Sensititre system indicating an overall 96.63% agreement, the exception being agreement of amoxicillin-clavulanic acid, combination antibiotics generally have lower concordance reproducibility of results around the breakpoint is poor[2]. ASTar system vs Multipoint concordance was lower in some cases: For example, Amoxicillin-clavulanate; displayed only 73.1% concordance, but of 52 data points, 22 had MICs of 8 or 16. Results with MICs close to breakpoints, such as this, are hard to reproduce and when excluding these data points, agreement increases to >90% and overall concordant interpretation increased from 93.47% to 95.16%. Time to reportable results was significantly reduced and average processing time per sample was 4 minutes. The ASTar system antibiogram results were >95% essential and categorical agreement with multipoint and Sensititre. 88 positive blood cultures were tested. Of which 82 were included on the ASTar panel. Of the remaining 6 positives; 1 was polymicrobial, 4 are not currently on the panel (3 anaerobes and 1 *Stenotrophomonas maltophilia*) and 1 was a laboratory error. The ASTar Gram negative organism panel covers >95% of the main organisms expected to cause a sepsis.

	ASTar system v Sensititre system	ASTar system v Multipoint
Antimicrobial	**MIC EA (%)**	**Concordant interpretation (%)**
Amikacin	98.4	-
Gentamicin	95.6	95.9%
Tobramycin	93.1	-
Ertapenem	100	-
Meropenem	97.3	100.0%
Cefepime	97.2	-
Cefotaxime	97.1	-
Cefoxitin	98.1	-
Ceftazidime	98.4	90.0%
Ceftazidime - Avibactam	90.4	-
Ceftolozane - Tazobactam	95.7	-
Ceftriaxone	98.6	-
Cefuroxime	98.2	91.8%
Cefazolin	95.2	-
Ciprofloxacin	97.1	91.9%
Levofloxacin	100	-
Co-trimoxazole	98.4	-
Aztreonam	98.6	97.1%
Amoxicillin - Clavulanic Acid	83.9	73.1%
Ampicillin	100	100.0%
Piperacillin - Tazobactam	95.8	94.9%
Colistin	100	100.0%
Tigecycline	100	-
TOTAL	**96.63**	

Table 1. Results summary on Gram negative isolates ASTar vs sensititre.

CONCLUSIONS

Key benefits

- Samples can be processed immediately after they flag as positive.
- Random access up to 12 samples for processing at any one time.
- Earlier access to results for critically ill patients.
- Average processing time of <4 minutes.

Performance

- The results generated by ASTar System were in agreement with Sensititre for 96.63% of all clinical samples processed.
- The results generated by ASTar System were in agreement with multipoint 95.16% of all clinical samples processed.
- Coverage of 95.4% of all organisms encountered during the study.

Ease of Use

- Intuitive user interface and simple load and go workflow which require minimal user training and expert knowledge.
- Automatic application of expert rules and exceptional phenotypes.
- Automated reading of results – significantly reduces the risk of reporting incorrect results due to human error.

REFERENCES

1. ISO 20776-2:2007 Clinical laboratory testing and in vitro diagnostic test Systems – Susceptibility testing of infectious agents and evaluation of performance of antimicrobial susceptibility test devices – Part 2. Evaluation of performance of antimicrobial susceptibility test devices.
2. Soares et al. Area of technical uncertainty for susceptibility testing of amoxicillin/clavulante against *E. coli:* analysis of automated system, Etest and disk diffusion methods compared to broth microdilution reference. Clinical Microbiology and Infection. 6th March 2020