The LIFETIMES Study – Interim Results from a Health and Economic Evaluation of a Rapid Phenotypic AST System
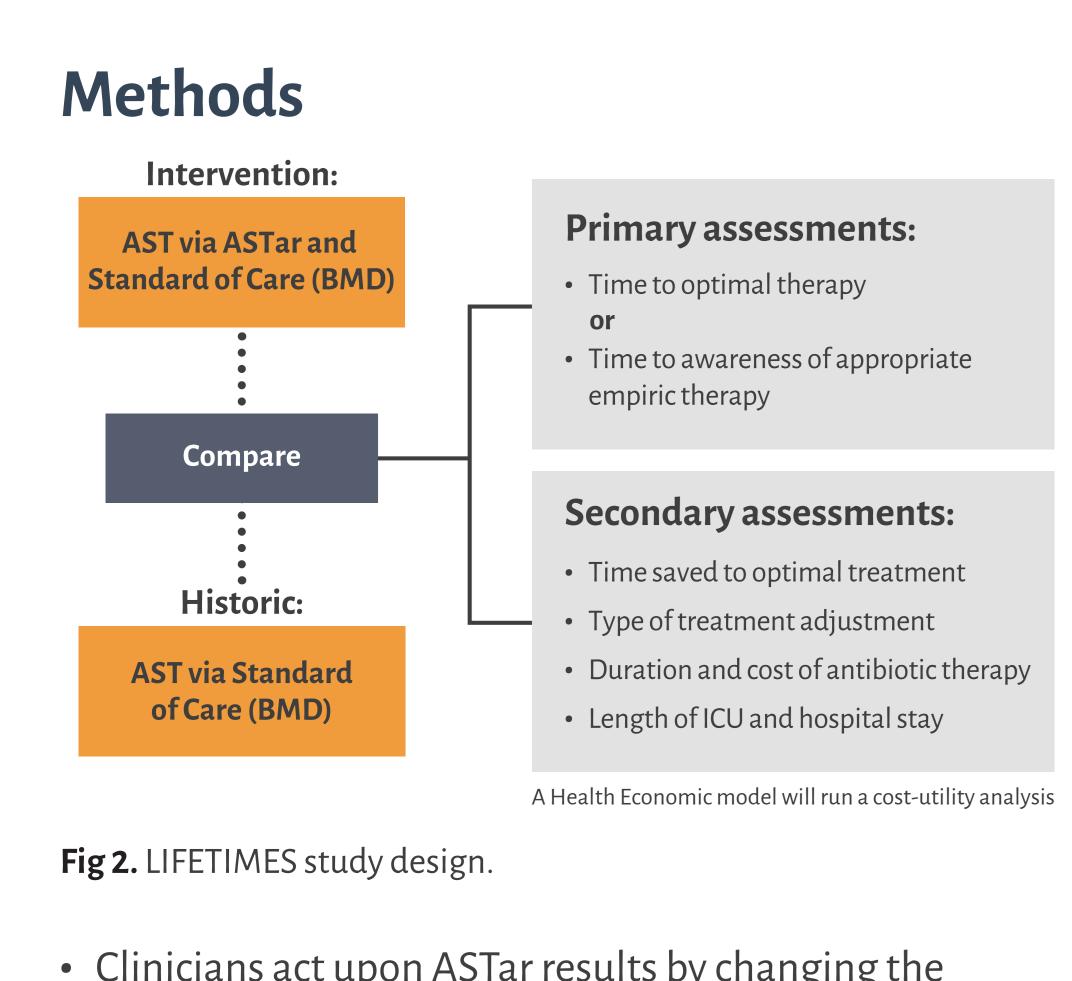
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Introduction

The fully automated ASTar® System tests directly from positive blood cultures and delivers AST results in approximately six hours[1] (Figure 1).

The LIFETIMES Health Economics and Outcomes Research (HEOR[2]) study is investigating the clinical impact of ASTar when managing ICU patients with Gram-negative Bloodstream Infections (BSIs) at four Italian sites with high incidence of antimicrobial resistance. Here, we present interim data from the LIFETIMES study.

Fig 1. ASTar Instrument.

Methods

Intervention:

Primary assessments:
- Time to optimal therapy
  or
- Time to awareness of appropriate empiric therapy

Secondary assessments:
- Time saved to optimal treatment
- Type of treatment adjustment
- Duration and cost of antibiotic therapy
- Length of ICU and hospital stay

A Health Economic model will run a cost-utility analysis

Fig 2. LIFETIMES study design.

- Clinicians act upon ASTar results by changing the antibiotic course or confirming appropriate empiric therapy. ASTar has been compared with standard of care and routine automated AST methods.

- So far, 48 patients have been enrolled – 48 were used for performance evaluation and 37 for clinical impact evaluation. Patient characteristics are shown in Table 1.

Table 1. Patient characteristics for all individuals in the clinical impact evaluation.

Patient characteristics	
Total patients (n)	
n = 37	
Age	
Median (IQR)	62.5 (46.8 to 73)
Minimum–maximum	0–85
Gender	
Male	29 (78%)
Female	8 (22%)
Score (median)	
SAPS (IQR)	40 (31.5 to 54)
SOFA (IQR)	8 (5.3 to 10)
CCI (IQR)	3 (2 to 5.8)
Time in hospital (days)	
Median (IQR)	20 (12 to 45)
Minimum–maximum	1–78
Time in ICU (days)	
Median (IQR)	17.5 (8.5 to 34)
Minimum–maximum	1–49
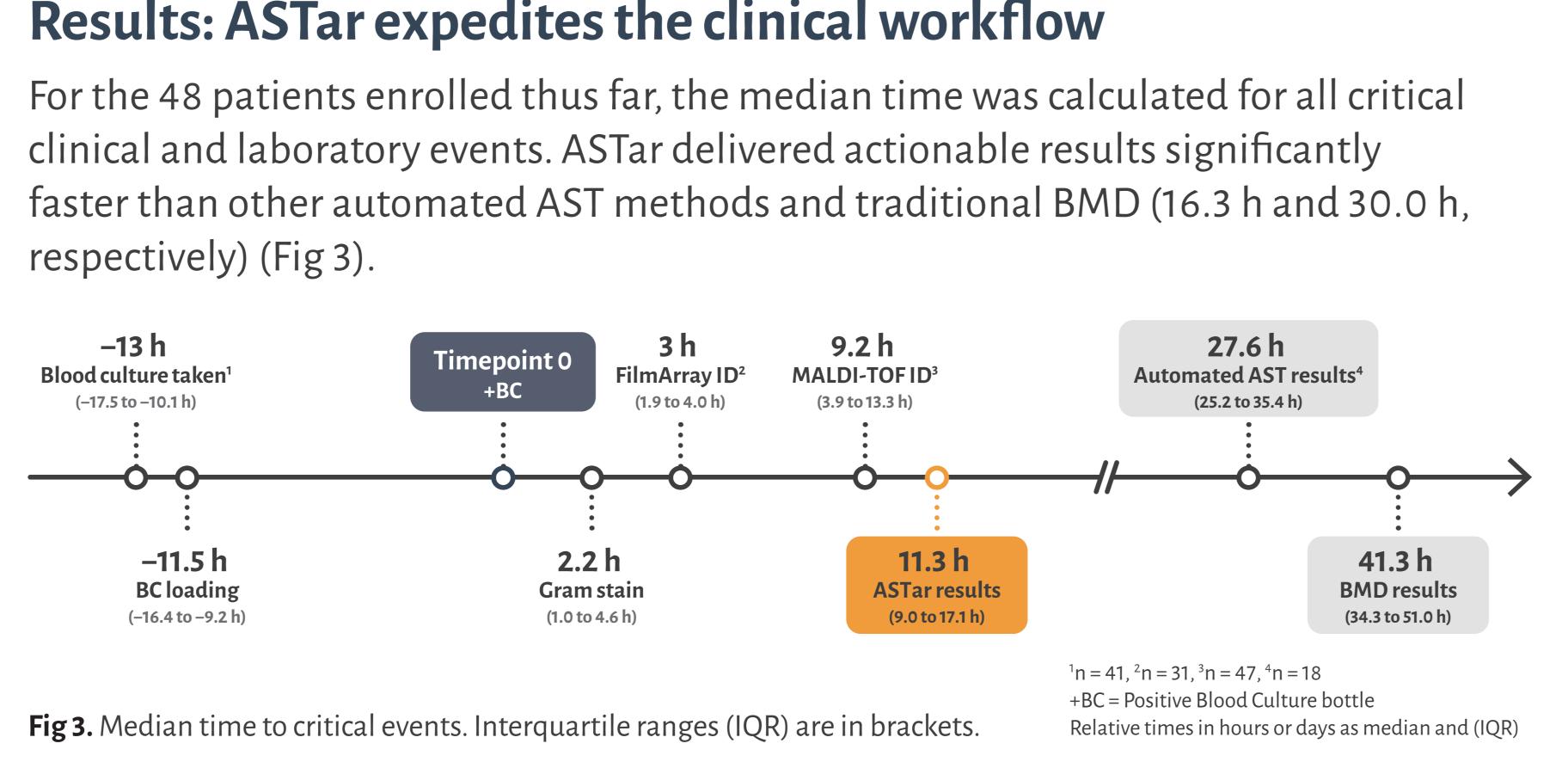
Results: ASTar expedites the clinical workflow

For the 48 patients enrolled thus far, the median time was calculated for all critical clinical and laboratory events. ASTar delivered actionable results significantly faster than other automated AST methods and traditional BMD (16.3 h and 30.0 h, respectively) (Fig 3).

Fig 3. Median time to critical events. Interquartile ranges (IQR) are in brackets.
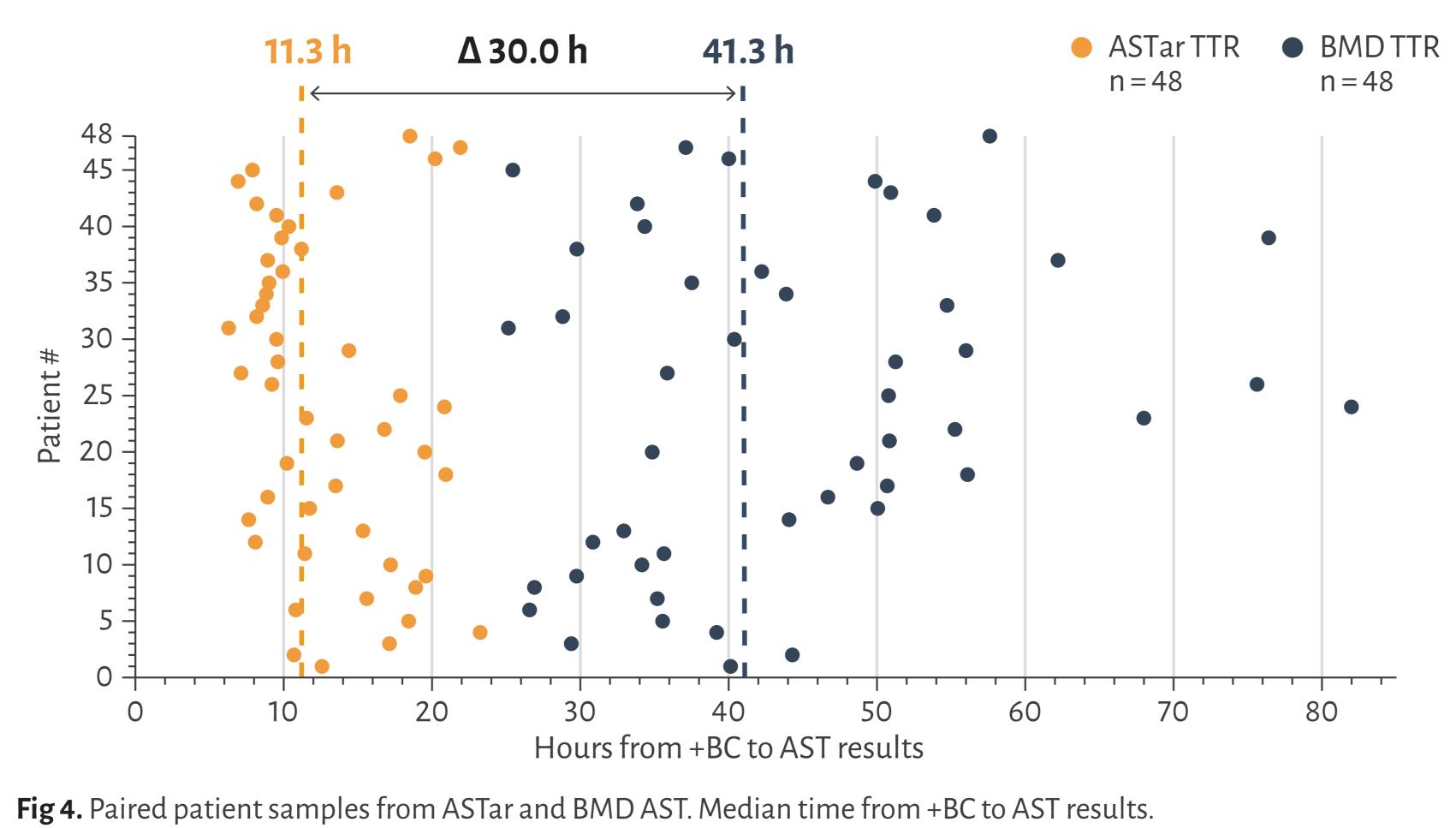
ASTar delivers actionable results >30 hours faster than BMD

Patient samples underwent AST using ASTar and traditional BMD. Median time from +BC to ASTar results was 11.3 h (6.3–23.2 h). Median time from +BC to BMD results was 41.3 h (25.1–82.0 h). The overall median time difference between the methods was 30.0 h (Fig 4).

Fig 4. Paired patient samples from ASTar and BMD AST. Median time from +BC to AST results.

ASTar drove antibiotic change in 43% of patient cases

For the 37 patients with complete case reports, we investigated how timely AST results via ASTar influenced treatment adjustment. In 43% (16/37) of patients, ASTar prompted antibiotic changes, with the type of antibiotic change dependent on the individual case.
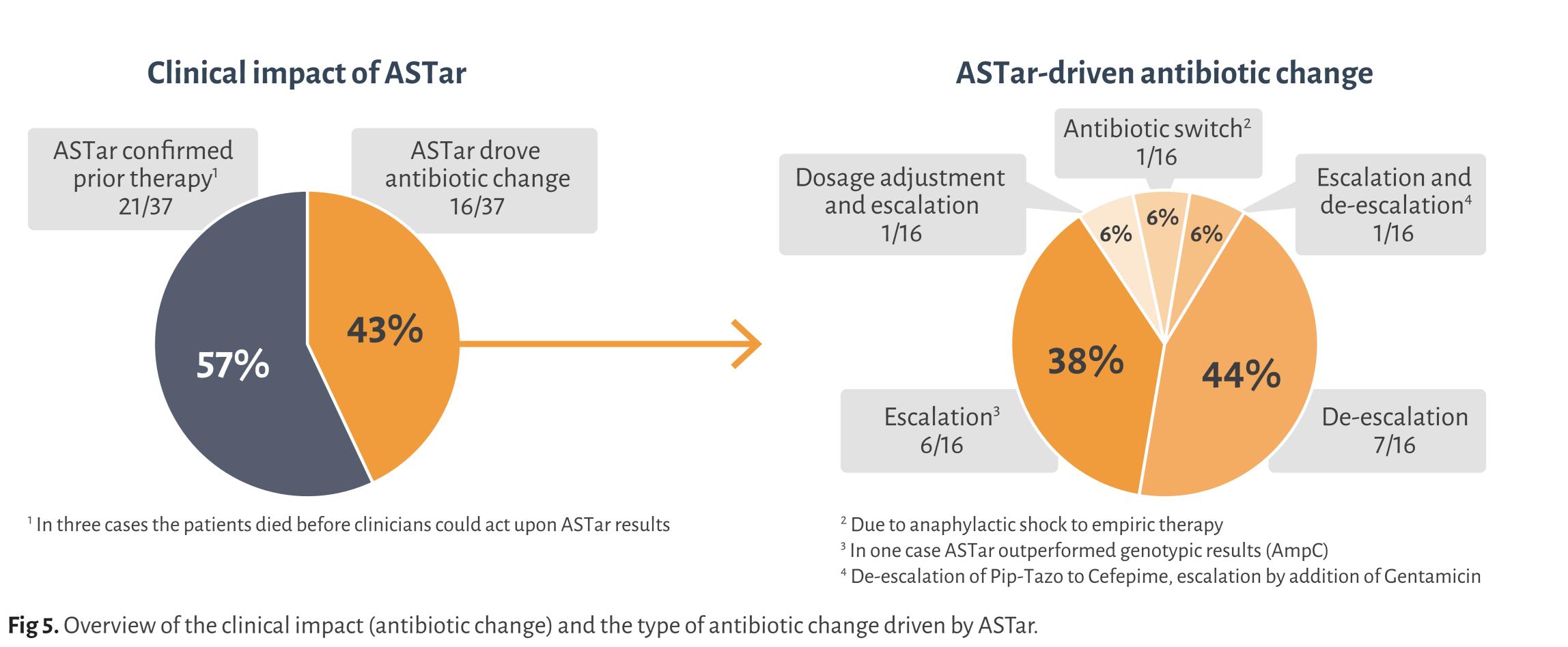
As demonstrated, ASTar can accurately guide multiple types of antibiotic adjustment. In 57% (21/37) of patients, ASTar confirmed prior therapy (Fig 5).

Clinical impact of ASTar

ASTar-driven antibiotic change

[1] In three cases the patients died before clinicians could act upon ASTar results

[2] Due to anaphylactic shock to empiric therapy
[3] In one case ASTar outperformed genotypic results (AmpC)
[4] De-escalation of Pip-Tazo to Cefepime, escalation by addition of Gentamicin

Fig 5. Overview of the clinical impact (antibiotic change) and the type of antibiotic change driven by ASTar.

ASTar performs at 94% total EA and above 94% total CA

For all tested antibiotics, MIC data was interpreted and assessed using EUCAST breakpoints v13.0[3].

ASTar maintained a high agreement with reference BMD methods, as assessed by an overall EA of 94.0%, CA of 94.3%, VMD rate of 3.1%, and MD rate of 1.9% (Table 2 and 3).

Table 2. Overall performance data. Essential Agreement (EA), Categorical Agreement (CA), Very Major Discrepancy (VMD), and Major Discrepancy (MD).

ASTar vs. traditional BMD			
EA #/tot (%)	CA #/tot (%)	VMD #/tot (%)	MD #/tot (%)
584/621 (94.0%)	578/613 (94.3%)	3/98 (3.1%)	9/485 (1.9%)

Note: Performance data above is generated with the CE-IVD marked version of ASTar BC G– Kit software. Panel and performance differs in the FDA cleared version of the ASTar BC G– Kit software available in US.

Table 3. Performance data for all antibiotics used in the study.

Antimicrobial agent	ASTar vs. traditional BMD	
	EA #/tot (%)	CA #/tot (%)
Amikacin	44/47 (93.6%)	45/47 (95.7%)
Amoxicillin-Clavulanic acid	20/23 (87%)	20/23 (87%)
Ampicillin	3/3 (100%)	3/3 (100%)
Aztreonam	12/12 (100%)	12/12 (100%)
Cefepime	37/39 (94.9%)	36/39 (92.3%)
Cefotaxime	9/9 (100%)	9/9 (100%)
Ceftazidime	32/41 (78%)	31/41 (75.6%)
Ceftazidime-Avibactam	41/44 (93.2%)	43/44 (97.7%)
Ceftolozane-Tazobactam	42/43 (97.7%)	43/43 (100%)
Ceftriaxone	24/26 (92.3%)	26/26 (100%)
Cefuroxime	5/5 (100%)	5/5 (100%)
Ciprofloxacin	44/47 (93.6%)	44/47 (93.6%)
Colistin	17/19 (89.5%)	19/19 (100%)
Ertapenem	31/31 (100%)	31/31 (100%)
Gentamicin	34/36 (94.4%)	35/36 (97.2%)
Levofloxacin	34/34 (100%)	23/26 (88.5%)
Meropenem	45/48 (93.8%)	45/48 (93.8%)
Piperacillin-Tazobactam	42/44 (95.5%)	40/44 (90.9%)
Tigecycline	7/7 (100%)	7/7 (100%)
Tobramycin	22/24 (91.7%)	22/24 (91.7%)
Trimethoprim-Sulfamethoxazole	39/39 (100%)	39/39 (100%)

Conclusion

- ASTar had an impact on 16 out of 37 patients (43%)

- ASTar shortens the median time from +BC to AST result by 30.0 hours when compared to traditional BMD and 16.3 hours when compared to other automated systems

- ASTar performance aligns with traditional BMD – overall EA and CA >90%

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. EUCAST. The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters, version 13.0, 2023.