Rapid AST enables treatment optimisation over 32 h earlier than standard of care for BSI patients: interim results of the LIFETIMES study

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Background

Health Economics and Outcomes Research (HEOR) studies assess whether new interventions improve health outcomes and cost-effectiveness over existing treatments (1).

The LIFETIMES HEOR study is a multicentre interventional investigation of ASTar®, a fully automated rapid Antimicrobial Susceptibility Testing (AST) system (Q-linea), for treatment of ICU patients with Gram-negative Bloodstream Infections (BSIs) (2). The system is compared to Standard of Care (SoC) methods, and clinicians act upon ASTar results by changing antibiotic therapy or confirming appropriate empiric therapy.

Here we present findings from the LIFETIMES study, focusing on the clinical impact of ASTar.

Materials and methods

- LIFETIMES is a multicentre study at four Italian ICUs comparing ASTar to historical controls (Table 1).
- In the interventional group, clinicians changed or continued antibiotic therapy based on ASTar results. The time to optimal therapy was calculated where antibiotic changes were made and time to awareness as time to communication of ASTar results.

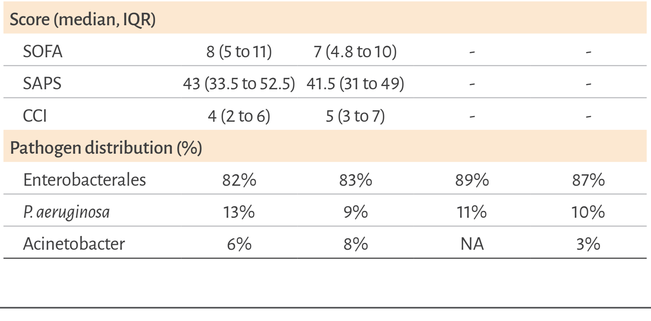

Fig 1. LIFETIMES study design.

Table 1. Patient characteristics at ICU admission for all individuals enrolled in this study.

	Adults		Paediatric	
	Cases	Historic	Cases	Historic
No of patients	87	100	28	40
Age yrs (median, IQR)	64 (56 to 73.5)	67 (56.8 to 75)	0.5 (0 to 6.3)	0 (0 to 1)
Gender				
Female	19 (21.8%)	37 (37%)	8 (28.6%)	16 (40%)
Male	68 (78.2%)	63 (63%)	20 (71.4%)	24 (60%)
Mechanical ventilation				
% invasive	82.8%	64%	70.4%	80%
% non-invasive	3.4%	6%	21.4%	10%
Sepis/septic shock				
% sepsis (no septic shock)	31%	33%	71.4%	57.5%
% sepsis (with septic shock)	49.4%	59%	21.4%	30%
Score (median, IQR)				
SOFA	8 (5 to 11)	7 (4.8 to 10)	-	-
SAPS	43 (33.5 to 52.5)	41.5 (31 to 49)	-	-
CCI	4 (2 to 6)	5 (3 to 7)	-	-
Pathogen distribution (%)				
Enterobacterales	82%	83%	89%	87%
P. aeruginosa	13%	9%	11%	10%
Acinetobacter	6%	8%	NA	3%

Conclusion

- ASTar significantly reduced median time from +BC to AST result by 32.8 hours compared to BMD and by 15.6 hours when compared to other automated systems
- Time to optimal treatment was significantly reduced by 20.4 hours versus SoC, with a trend towards reducing total sum of days on antibiotics for adult patients
- ASTar guided change in antibiotic therapy occurred in 23% (26/115) of all patients (22% of adult cases, 25% of paediatric cases) and confirmed prior therapy sooner than SoC in the remaining 77%

Results

ASTar expedites the clinical workflow

Median time to laboratory and microbiology events from index time 0 (+BC) was calculated. ASTar delivered actionable results significantly faster than other automated AST methods (median 15.6 h faster with ASTar) and traditional BMD (median 32.8 h faster with ASTar) (Fig 2).

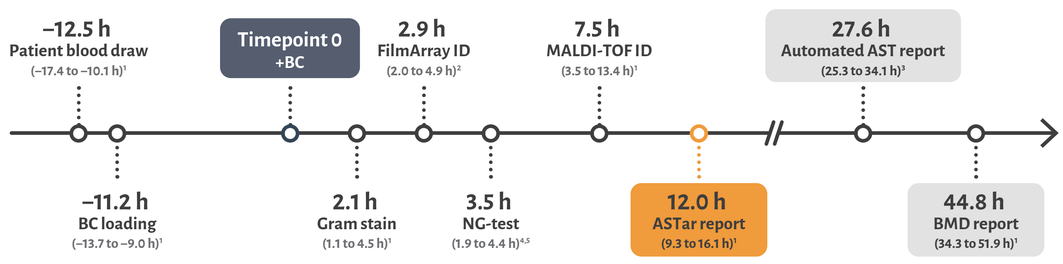

Fig 2. Median time to laboratory and microbiology events. All time difference are from index time = 0 (positive blood culture [+BC]). Interquartile ranges (IQR) are in brackets. [1]n=115, [2]n=66, [3]n=35, [4]n=38, [5]CTX-M Multi and Carba-5.

ASTar delivered actionable results 32 h faster than BMD and reduced time to optimal treatment by 20 h vs. SoC

Patient samples underwent AST using both ASTar and traditional BMD with overall ASTar results provided a median of 32.8 h faster than BMD. Median time from +BC to ASTar result was 12.0 h (IQR: 9.3–16.1) and to BMD was 44.8 h (IQR: 34.3–51.9) (Fig 3).

Faster time to results (TTR) enabled earlier change to optimal treatment (time from blood draw to optimal treatment [TTOT]) by over 20 h vs. historic SoC, 25.7 h (IQR: 21.0–35.7) in adult cases, compared to 46.1 (IQR: 37.2–64.2) in adult historics; and 48.1 (IQR: 31.8–96.3) in paediatric cases, compared to 70.0 (IQR: 48.8–97.2) in paediatric historics (Fig 4).

By providing a faster TTR and TTOT, ASTar demonstrated a trend in reduction of total time on (individual) antibiotics for the adult patient cohort (Table 2).

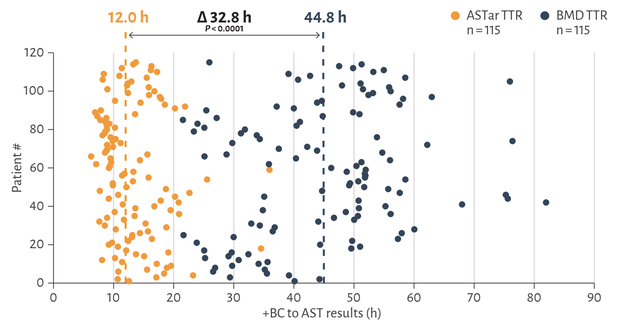

Fig 3. Paired patient samples for time to result (TTR) for ASTar and BMD AST. Median time from +BC (time 0) to AST results. Wilcoxon matched-pairs signed-rank test.

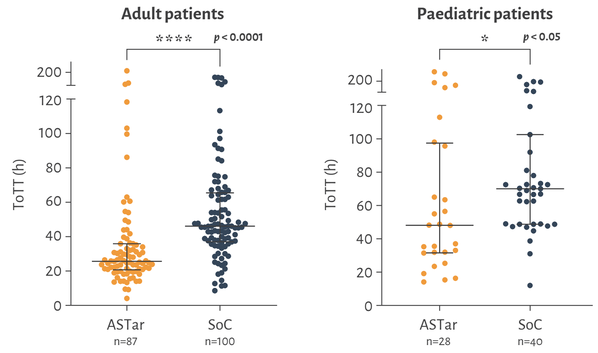

Fig 4. Age-group match comparison of time to optimal treatment or awareness of treatment TTOT for ASTar case patients vs. historic patients/ SoC. Median time (IQR). Mann-Whitney test.

Table 2. Duration of antibiotic therapy in adults for ASTar cases and historical controls (SoC). Median (IQR). Consecutive: days calculated from the start date of first antibiotic to end date of final antibiotic. Total days on individual antibiotics. Ongoing analysis for paediatric patients.

Adult patients				
Antibiotic therapy	Cases (ASTar, n=87)	Historic (SoC, n=100)	Reduction	Order of individual antibiotics
Consecutive days	7.4 (5.2–11.2)	9.8 (6.0–14.0)	2.4 days/57 h	Abx A, Abx B, Abx C
Total days	9.4 (5.9–13.9)	10.9 (6.9–18.6)	1.5 days/36 h	Abx A, Abx B, Abx C

ASTar drove antibiotic modifications in 23% of patient cases

Among the 115 enrolled patients, timely ASTar results guided antibiotic therapy adjustments. ASTar accurately guided antibiotic changes in 23% (26/115) of all patients (22% adults [19/87], 25% paediatrics [7/28]). For the remaining 77% (89/115), ASTar promptly confirmed prior therapy, much earlier than standard of care (SoC) methods (Fig 5).

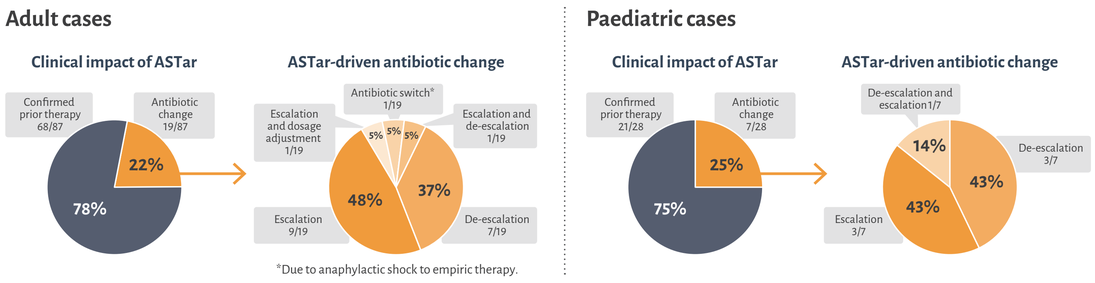

Fig 5. Antibiotic changes and type of antibiotic change upon availability of ASTar results.

ASTar performed at > 93% total EA and > 94% total CA

MIC data was interpreted and assessed for all tested antibiotics using EUCAST breakpoints v14.0 (3).

ASTar maintained a high agreement with reference BMD methods, as indicated by an overall EA of 93.2% and CA of 94.9%, VMD rate of 2.1%, and MD rate of 2.5% (Table 3).

Table 3. 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 (%)
1010/1084 93.2%	1027/1082 94.9%	4*/190 (2.1%)	21/825 (2.5%)

*6/190 VMDs; however, two cases were not counted as VMDs as they were within EA at breakpoint. *K. pneumoniae*/*Piperacillin-tazobactam* (MICs 8, 16), and *P. mirabilis*/Gentamicin (MICs 2, 4).

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