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Rapid AST enables treatment optimization over 1.3 days faster for BSI patients – 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 multicenter 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.

For patients with bloodstream infections (BSIs) and sepsis, cost-effective and timely antimicrobial susceptibility testing (AST) is crucial (3–4).

Here we present findings from the LIFETIMES study, focusing on the clinical impact of ASTar, and two patient cases where ASTar has guided antimicrobial treatment optimization.

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Materials and methods

- LIFETIMES is a multicenter 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.

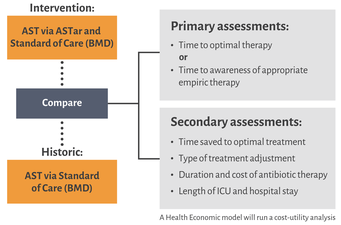


Fig 1. LIFETIMES study design.

Table 1. Patient characteristics for individuals enrolled in this study.

	Adults		Pediatric	
	Cases	Historic	Cases	Historic
No. of patients	55	100	28	40
Age yrs (median, IQR)	68 (58 to 74)	67 (56.8 to 75)	0.5 (0 to 6.3)	0 (0 to 1)
Gender				
Female	16 (29.1%)	37 (37%)	8 (28.6%)	16 (40%)
Male	39 (70.9%)	63 (63%)	20 (71.4%)	24 (60%)
Mechanical ventilation				
% invasive	80.0%	64%	71.4%	80%
% non-invasive	5.5%	6%	21.4%	10%
Sepsis/septic shock				
% sepsis (no septic shock)	29.1%	33%	71.4%	57.5%
% sepsis (with septic shock)	56.4%	59%	21.4%	30%
Score (median, IQR)				
SOFA	8 (5 to 10)	7 (4.8 to 10)	-	-
SAPS	42 (33 to 54)	41.5 (31 to 49)	-	-
CCI	4 (2 to 6)	5 (3 to 7)	-	-
Pathogen distribution (%)				
Enterobacterales	83.6%	83%	89.3%	87.5%
Pseudomonas	10.9%	9%	10.7%	10%
Acinetobacter	5.5%	8%	NA	2.5%

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 14.5 h faster) and traditional BMD (median 33.1 h faster) (Fig 2).

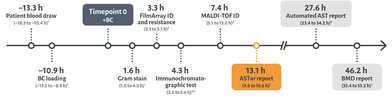


Fig 2. Median time to critical laboratory and clinical events. All times relative to positive blood culture (+BC). Interquartile ranges (IQR) are in brackets. [1]n=83, [2]n=44, [3]n=22, [4]n=33, [5]CTX-M Multi and Carba-5, [6]n=82.

ASTar delivered actionable results 33 h faster than BMD and reduced time to optimal treatment by over 16 h vs. SoC

Patient samples underwent AST using both ASTar and traditional BMD, with overall ASTar results provided a median of 33.1 h faster than BMD. Median time from +BC to ASTar result was 13.1 h (IQR: 9.8–16.6), compared to 46.2 h for BMD (IQR: 35.4–53.2) (Fig 3).

Faster time to results (TTR) enabled earlier adjustment to optimal treatment (time from blood draw to optimal treatment [TTOT]), with a reduction of over 16 h vs. historic SoC. In adult cases, median TTOT was 29.5 h (IQR: 23.6–39.7), compared to 46.1 (IQR: 36.9–64.6) in adult historic cases. In pediatric cases, median TTOT was 48.1 (IQR: 31.6–97.4) with ASTar, compared to 70.0 (IQR: 48.8–102.5) in pediatric historic cases (Fig 4).

By delivering a faster TTR and TTOT, ASTar showed a trend toward reducing total time spent on (individual) antibiotics in the adult patient cohort (Table 2).

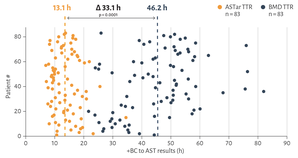


Fig 3. Paired patient samples for time to result (TTR) for ASTar and BMD AST. Median time from +BC (time 0) to AST results. Wilcoxon matched-pairs signed-rank test.

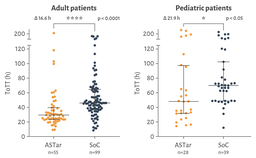


Fig 4. Age-group match comparison of time to optimal treatment or awareness of treatment (TTOT) for ASTar case patients vs. historic patients/SoC. Median time (IQR). Mann-Whitney test.

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 pediatric patients.

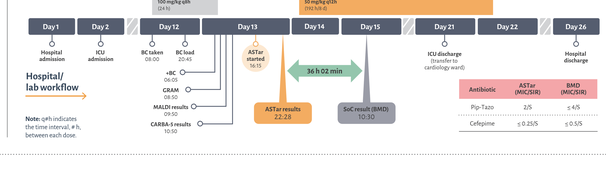
Adult patients				
Antibiotic therapy	Cases (ASTar, n=55)	Historic controls (SoC, n=100)	Reduction	Order of individual antibiotics
Consecutive days	6.9 (3.6–10.5)	9.7 (6.0–13.8)	2.9 days/70 h	Abx A, Abx B, Abx C
Total days	8.3 (5.7–13.3)	10.8 (6.9–18.2)	2.5 days/60 h	Abx A, Abx B, Abx C

Pediatric case 1: ASTar-driven antibiotic change of Piperacillin-Tazobactam to Cefepime 36 hours earlier than SoC

Patient characteristics

A < 1-year-old female infant was admitted to the ICU due to cardiopathy.

- BSI associated with a central venous catheter, and sepsis
- Placed on invasive mechanical ventilation
- **Pathogen ID:** *Enterobacter cloacae* complex



ASTar-driven antibiotic therapy

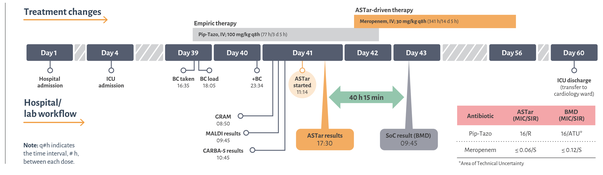
- ASTar drove treatment change which was optimal (correct coverage and dosage)
- Change from Piperacillin-Tazobactam to Cefepime possible 36 hours earlier than SoC
- Patient suffered no side effects from the treatment and was discharged from the hospital following clinical cure of the infection

Pediatric case 2: ASTar-driven antibiotic change of Piperacillin-Tazobactam to Meropenem 40 hours earlier than SoC

Patient characteristics

A < 1-year-old male infant was admitted to the ICU due to cardiopathy.

- BSI associated with a central venous catheter, and sepsis
- Placed on invasive mechanical ventilation
- **Pathogen ID:** *Enterobacter cloacae* complex



ASTar-driven antibiotic therapy

- ASTar drove treatment change which was appropriate (correct coverage)
- Escalation of Piperacillin-Tazobactam to Meropenem possible 40 hours earlier than SoC
- Patient suffered no side effects from the treatment and was discharged from the hospital following clinical cure of the infection

ASTar drove antibiotic modifications in 1 in 4 patients

Among the 83 enrolled patients, timely ASTar results guided antibiotic therapy adjustments. ASTar accurately guided antibiotic changes in 29% (24/83) of all patients (31% adults [17/55], 25% pediatrics [7/28]). In the remaining 71% (59/83), ASTar confirmed prior therapy, but significantly earlier than standard of care (SoC) methods (Fig 5).

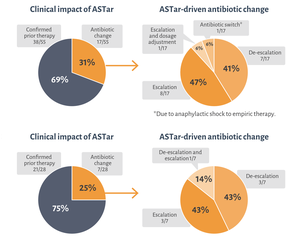


Fig 5. Antibiotic changes and type of antibiotic change upon availability of ASTar results.

ASTar performed at 94% total EA and > 95% total CA

ASTar maintained a high agreement with reference BMD methods, as evidenced by an overall EA of 94.0%, CA of 95.3%, VMD rate of 2.6%, and MD rate of 2.0% (Table 3). MIC data for all tested antibiotics was interpreted using EUCAST breakpoints v 14.0 (5).

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 (%)
757/805	766/804	3*/114	13/641
94.0%	95.3%	(2.6%)	(2.0%)

*5/114 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*/Centamicin (MICs 2, 4).

Conclusions

- ASTar reduced the median time from +BC to AST results by 33.1 hours vs. BMD, and by 14.5 hours compared to other automated systems
- Time to optimal treatment was reduced by at least 16 hours compared to SoC, with a trend toward fewer total days on antibiotics for adult patients
- ASTar-guided antibiotic changes were made in 29% (24/83) of all cases (31% of adult cases, 25% of pediatric cases), while in the remaining 71%, ASTar confirmed prior therapy earlier than SoC
- In the pediatric patient case examples, ASTar guided earlier optimization of antimicrobial therapies compared to SoC methods, with time savings of 36–40.25 hours
- ASTar supported timely escalation, de-escalation, and optimization of antimicrobial therapies, and its integration into clinical workflows facilitated faster decision-making with potential to improve patient care

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