Rapid AST expedites antimicrobial therapy optimisation in BSI patients - clinical cases from the LIFETIMES HEOR study

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Background

For patients with bloodstream infections (BSIs) and sepsis, cost-effective and timely antimicrobial susceptibility testing (AST) is crucial¹⁻⁴.

Health and Economic Outcomes Research (HEOR) studies determine whether a new intervention outweighs existing treatments in terms of both cost and health outcomes⁵.

The ongoing LIFETIMES HEOR study is a prospective, interventional evaluation assessing the benefits of using ASTar®, a fully automated, rapid phenotypic AST System⁶, in the ICU for patients with Gram-negative BSIs. In this study, clinicians act upon ASTar results by changing the antibiotic course or confirming appropriate empiric therapy. Here, we present three patient cases from the LIFETIMES study where ASTar has guided antimicrobial treatment optimisation.

Conclusion

- ASTar guided optimisation of antimicrobial therapies sooner than Standard of Care methods, resulting in median time savings of 28.5 hours
- ASTar proves invaluable during the escalation, de-escalation, or optimisation of empiric therapies
- Integrating ASTar into the clinical workflow helps expedite clinical decision-making, earlier administration of appropriate antimicrobial therapies, and could improve patient care

Case 1: ASTar-driven escalation of Cefepime to Ceftazidime-Avibactam 16 hours earlier than SoC

Patient characteristics A 48-year-old male was admitted to the ICU with polytrauma related to severe traumatic brain injury and lung failure. BSI of unknown origin and septic shock.

- **SOFA score:** 9
- SAPs score: 40
- **Pathogen ID:** Enterobacter cloacae complex

Treatment changes **Empiric therapy ASTar-driven therapy** Cefepime, IV; 3 g loading dose Ceftazidime-Avibactam, IV; 2.5 g loading dose + 2 g q8h continuous infusion + 2.5 g q8h continuous infusion (16 h 18 min) (50 h 22 min) Day 1 Day 3 Day 4 Day 2 0 16 h ASTar +BC MALDIID **BC LOAD** 19:56 08:59 started 08:35 12:47 0-Hospital/ GRAM **FilmArray ID Note:** q#h indicates SoC result (BMD) **ASTar results** 22:30 23:53 lab workflow the time interval, # h, 19:10 11:07 between each dose.

ASTar-driven antibiotic therapy

- ASTar drove treatment escalation which was optimal (correct coverage and dosage).
- Escalation from Cefepime to Ceftazidime-Avibactam.
- The treatment adjustment was 16 hours earlier than SoC.
- The patient suffered no side effects from the treatment and was discharged from the hospital following clinical cure of the infection.

Case 2: ASTar-driven de-escalation of Piperacillin-Tazobactam to Ceftriaxone >37 hours earlier than SoC

Patient characteristics	Treatment changes	Empiric therapy ASTar-	driven therapy			•
A 77-year-old female was admitted to the ICU with septic shock (right renal lithiasis and right hydronephrosis).		Piperacillin-Tazobactam, IV; 4.5 g q8h (7 h)Ceftriaxone, IV; 2 g q12h (154 h 16 min)				
	Day 1	Day 2	Day 3	Day 4	Day 9	•

ASTar-driven antibiotic therapy

- ASTar drove treatment de-escalation which was optimal (correct microbial coverage).
- De-escalation from Piperacillin-Tazobactam to



Case 3: ASTar-driven dosage and treatment adjustment >28 hours earlier than SoC





ASTar-driven antibiotic therapy

- ASTar drove treatment adjustment which was optimal (correct coverage and dosage).
 - Meropenem dosage was reduced to avoid toxicity.
 - Ciprofloxacin was then administered as a combination therapy.
- The treatment adjustment was 28.5 hours earlier than SoC.
- The patient suffered no side effects from the treatment and there was clinical cure of the infection.

Materials and methods

The HEOR study spans four sites across Italy and ICU patients with a Gram-negative BSI are prospectively enrolled in this study – 45/160 patients have been enrolled to date. Patient samples undergo AST using both ASTar and Standard of Care (SoC) methods (BMD) and clinicians make treatment adjustments based on ASTar results.

Descriptive case studies highlighting clinical presentation, microbiological findings, treatment regimens, and patient outcomes have been created to investigate the impact ASTar has on individual patients.

Primary objectives: measure time to optimal antimicrobial therapy or time to awareness of appropriate non-modifiable empiric therapy.

Secondary assessments: time saved, type of treatment adjustment, and duration of antimicrobial therapy.

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