The Landscape of *Pseudomonas aeruginosa* Clinical Isolates in Rural Northeastern U.S. and the Potential Impact on Hospital Mortality

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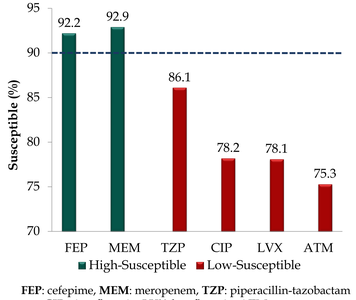
Introduction

- Mortality within 24-72 hours occurs in up to 50% of patients diagnosed with *P. aeruginosa* bacteremia, highlighting the importance of appropriate empiric therapy.[1,2]
- In 2016, the use of 2 antipseudomonal antibiotics from different classes is suggested when empirically treating organisms with local susceptibility of < 90% to an agent being considered for monotherapy.[3]
- An increase in mortality risk has been associated with delays in time-to-antibiotic administration in patients with sepsis and septic shock.[4,5]
- Although mortality benefits with combination therapy has not been fully elucidated, the use of combination therapy has been employed for three (3) main reasons: *in vitro* antibiotic synergy, preventing resistance emergence, and increasing the likelihood of providing an active agent in the initial empiric regimen against *P. aeruginosa*.[6]

Methods

- A retrospective, cohort analysis conducted to assess outcomes of patients with *P. aeruginosa* bloodstream infections treated at Eastern Maine Medical Center (EMMC) in Bangor, ME and Maine Medical Center (MMC) in Portland, ME between January 2013 and December 2015.
- Definitions:
  - High-susceptibility agent ≥ 90% susceptible to *P. aeruginosa*
  - Low-susceptibility agent < 90% susceptible to *P. aeruginosa*
- Susceptibility of each agent to *P. aeruginosa* determined by all non-duplicate clinical isolates obtained at EMMC and MMC from January 1, 2015 to December 31, 2015.
- Data collected include demographics, antimicrobial therapy, and outcome parameters.
- Descriptive statistics (student's *t*-test, Chi-squared (χ^2) test) was performed on demographic data.
- Cox proportional hazard regression performed to assess time-to-death during hospitalization between low- and high-susceptibility isolates.
- Stata/IC 14.2 for Windows was used for statistical analysis (StataCorp LLC, College Station, TX).
- All manual and automated susceptibility data and patient data collection were managed through REDCap software (hosted by Vanderbilt University).

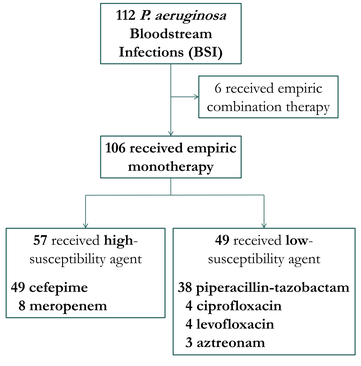
Figure 1. Susceptibility Distribution



FEP: cefepime, **MEM**: meropenem, **TZP**: piperacillin-tazobactam
CIP: ciprofloxacin, **LVX**: levofloxacin, **ATM**: aztreonam

- Aggregate data for *P. aeruginosa* from EMMC and MMC
- Isolates (*n*=362) collected between Jan 1, 2015-Dec 31, 2015

Figure 2. Patient Allocation



Results

Table 1. Patient Demographics

	Low, n = 49	High, n = 57	*p*
Age (years), median (IQR)	71 (62-80)	68 (57-74)	0.160
Male, n (%)	38 (78)	35 (61)	0.073
Weight (kg), median (IQR)	83.4 (68.9-93)	81.4 (65.8-98.6)	0.932
EMMC, n (%)	30 (61)	38 (67)	0.560
Pitt Bacteremia Score, median (IQR)	2 (1-3)	2 (1-3)	0.340
Admission Type			0.941
Home, n (%)	33 (67)	38 (67)	
Nursing facility, n (%)	6 (12)	6 (11)	
ICU admission, n (%)	21 (43)	19 (33)	0.313
Nosocomial, n (%)	13 (27)	12 (21)	0.508

Table 2. Outcome Parameters

	Low, n = 49	High, n = 57	*p*
In-Hospital Mortality, %	13.2	8.5	0.111
Resistance to Empiric Therapy, n (%)	5 (10)	1 (2)	0.093
Duration of Therapy, median days (IQR)	6 (4-8)	8 (6-13)	0.008
Hospital Length of Stay, median days (IQR)	7 (5-11)	9 (6-21)	0.033
Duration of Bacteremia, median days (IQR)	2 (2-3)	2 (1-4)	0.364

- Overall, in-hospital mortality in our patient population was 22% (23/106).

Figure 3. Infection Source

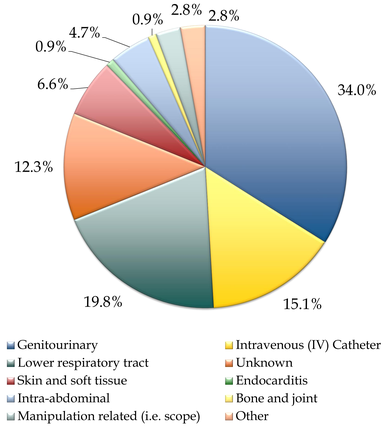


Figure 4. Prescribed Empiric Antimicrobials

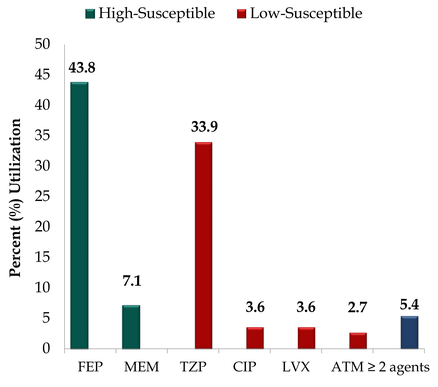
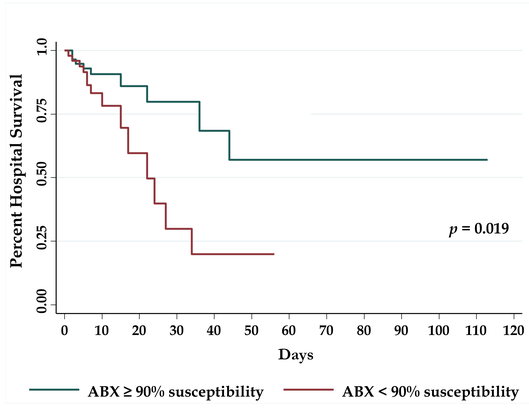


Figure 5 & Table 3. Survival of Patients Treated with Monotherapy Antipseudomonal



Covariates	Hazard ratio, 95% CI	*p*
Low Susceptibility	2.85 (1.19,6.87)	0.019
Age	0.99 (0.96,1.02)	0.505
Male gender	0.93 (0.36,2.42)	0.885

Cox proportional hazard regression analysis showed patients treated empirically with a high-susceptible monotherapy agent were more likely to survive than patients treated with a low-susceptible agent.

Discussion and Conclusion

- Most patients with eventual *P. aeruginosa* BSI at EMMC and MMC received monotherapy antipseudomonal (95%) for empiric therapy.
- In-hospital mortality did not occur significantly more often in patients who received a low-susceptibility antipseudomonal antimicrobial (13.2% vs. 8.5%, $p = 0.111$).
- Patients treated with a low-susceptibility antipseudomonal were 2.8 times more likely to experience in-hospital mortality rate than those who were treated with a high-susceptibility antipseudomonal antimicrobial.
- Considerations of pharmacokinetics and pharmacodynamics was not collected and accounted for in both cohorts.
- Robust risk-stratification can lead to appropriate identification of patients who may benefit from treatment with a high-susceptibility antipseudomonal agent, or if contraindicated, treatment with combination therapy that includes a low-susceptibility antipseudomonal agent.

Disclosures

MW: Nothing to disclose.
AMC: Consultant for Cerexa subsidiary of Allergan, Grant Investigator for Cerexa subsidiary of Allergan, Cubist Pharmaceuticals, wholly owned subsidiary of Merck, Michigan Department of Community Health, Forest Laboratories subsidiary of Allergan, Astellas Pharmaceuticals Inc. and Scientific Advisor for The Medicine's Company.

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