Re-Evaluation of cefepime or piperacillin-tazobactam to Decrease Use of Carbapenems in ESBL-producing Enterobacterales BloodStream Infections (REDUCE-BSI)

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INTRODUCTION

- Rates of ESBL-producing Enterobacterales (ESBL-E) have increased to 24% globally, and rates of carbapenem (CBP)-resistant Enterobacterales in endemic regions have reached as high as 65%[1,2]
- The role of non-carbapenems (NCBP) in ESBL-E as CBP-sparing alternatives is widely debated
- This study sought to re-examine patient outcomes associated with piperacillin-tazobactam (PTZ) and cefepime (FEP) for ESBL-E bloodstream infections (BSI)

METHODS

- Single center, retrospective chart review conducted at a 1,111-bed tertiary academic medical center from July 2016 to July 2019
- Inclusion criteria: adults admitted to the hospital with an ESBL-E BSI
- Exclusion criteria
  - Treatment with antibiotics other than meropenem, ertapenem, piperacillin-tazobactam, cefepime
  - Received antibiotics for < 24 hours
  - Polymicrobial bacteremia
  - Received concomitant antibiotic therapy for another gram-negative (non-ESBL) infection
- Primary outcome: in-hospital mortality
- Secondary outcomes: clinical cure, microbiologic cure, infection recurrence, and resistance development

RESULTS

Figure 1. Patient Enrollment by Study Drug

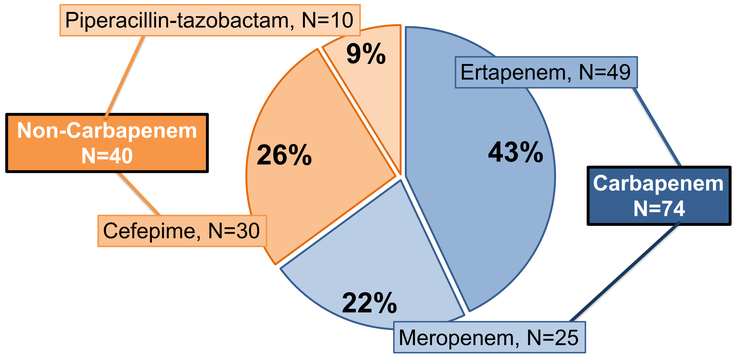

Table 1. Comparison of Baseline Characteristics

	CBP, N=74	NCBP, N=40
Age (years), mean ± SD	61 ±15	63 ±17
Male, n (%)	42 (57%)	21 (53%)
White, n (%)	48 (65%)	32 (80%)
Admit Weight (kg), median (IQR)	79 (66-90)	78 (63-89)
Charlson Index, median (IQR)	3 (2-5)	3 (1-5)
Pitt Score ≥4, n (%)	19 (26%)	6 (15%)
ICU Admission, n (%)	34 (46%)	16 (40%)
ID Consult, n (%)*	63 (85%)	27 (68%)
Genitourinary Source, n (%)	42 (57%)	22 (55%)
Concomitant Infection, n (%)	25 (34%)	8 (20%)
Source Control at 72h, n (%)	14 (19%)	5 (13%)
Organism, n (%)		
Klebsiella spp.	24 (32%)	14 (35%)
E. coli	50 (68%)	26 (65%)
Beta-lactam TDM, n (%)	12 (16%)	9 (23%)
Length of Stay (days), median (IQR)	12 (6-21)	10 (5-20)
Length of Therapy (days), median (IQR)	9 (7-13)	9 (6-11)
Combination Therapy, n (%)	14 (19%)	3 (8%)

* P value was statistically significant; TDM: Therapeutic Drug Monitoring

Figure 2. Histogram of Cefepime and Piperacillin-Tazobactam MIC

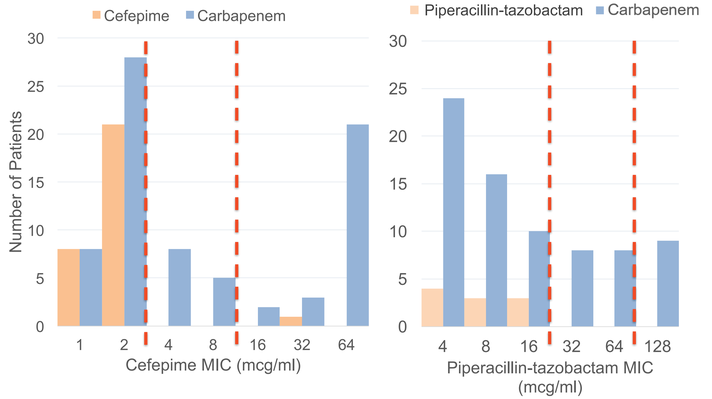

Figure 3. Primary and Secondary Outcomes

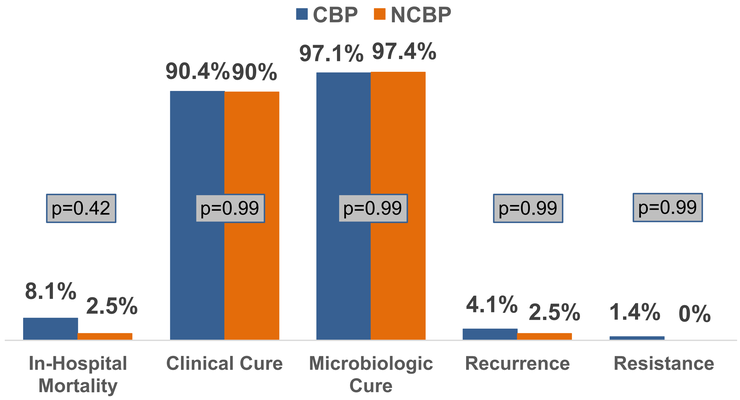

Table 2. Subgroup Analyses for In-Hospital Mortality

	CBP	NCBP	P value
Pitt ≥ 4	3/19 (15.8%)	1/6 (16.7%)	0.99
ICU Admission	5/34 (14.7%)	1/16 (6.3%)	0.65
Non-genitourinary Source	6/32 (18.8%)	1/18 (5.6%)	0.40
Combination Therapy	5/14 (35.7%)	0/3 (0%)	0.51

STRENGTHS

- Large number of patients treated definitively with cefepime
- Inclusion of population similar to previous ESBL-E studies, and therefore easily comparable
- Collection of detailed descriptive data, including dosing regimens, MIC data, TDM, and source control

CONCLUSION

- This cohort was not able to detect a difference for in-hospital mortality in patients treated with cefepime or piperacillin-tazobactam compared to carbapenems in ESBL-producing *E. coli* and *Klebsiella* spp. BSI
- These observations support the use of cefepime and piperacillin-tazobactam in ESBL-E when isolates are fully susceptible as a strategy to reduce unnecessary carbapenem consumption and preserve their antimicrobial activity

CONTACT/ REFERENCES

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2. Logan LK, Weinstein RA. J Infect Dis. 2017; 215(suppl_1):S28-36.