β-lactam/β-lactamase inhibitors

- 6 retrospective cohort studies in patients with ESBL *Escherichia coli* bacteremia
- 192 patients, divided into empiric and definitive cohorts
  - 103 in empiric; 72 BLBLI and 31 carbapenem cohort
  - 174 in definitive; 54 BLBLI and 120 carbapenem

β-lactam/β-lactamase inhibitors

Table 2. Characteristics of Patients With Bloodstream Infections (BSIs) Caused by Extended-Spectrum β-Lactamase–Producing *Escherichia coli*, According to Therapy[a]

	Empirical Therapy Cohort			Definitive Therapy Cohort		
Characteristic	BLBLI (n = 72)	Carbapenem (n = 31)	*P*	BLBLI (n = 54)	Carbapenem (n = 120)	*P*
Age, median y (IQR)	69 (59–80)	60 (52–78)	.1[b]	67 (56–83)	70 (55–78)	.3[b]
Male sex	29 (40.3)	11 (35.5)	.6	34 (63)	70 (58.3)	.5
Nosocomial acquisition	26 (36.1)	24 (77.4)	<.001	18 (33.3)	67 (55.8)	.006
Charlson index, median, (IQR)	2 (1–5)	2 (1–5)	.6[b]	2.5 (1–5)	3 (1–5)	.5[b]
Cancer	21 (31.9)	11 (35.5)	.7	15 (27.8)	43 (35.8)	.2
Immunosuppression	5 (6.9)	5 (16.1)	.1[c]	3 (5.6)	15 (12.5)	.1
Neutropenia	2 (2.8)	3 (9.7)	.1[c]	0	7 (5.8)	.1[c]
Urinary or biliary tract as source	52 (72.2)	18 (58.1)	.1	42 (77.8)	79 (65.8)	.1
ICU admission	7 (9.9)	2 (6.7)	.7[c]	4 (7.4)	18 (15.4)	.1
Severe sepsis or shock at presentation	14 (19.4)	9 (29.0)	.2	8 (14.8)	32 (26.7)	.08
Pitt score, median (IQR)	1 (0–2)	1 (0–2)	.7[b]	1 (0–2)	1 (1–2)	.04[b]
CTX-M enzyme	57 (80.3)	25 (86.2)	.4	43 (82.7)	95 (81.2)	.8
Definitive therapy						
Carbapenem	32 (44.4)	30 (93.7)	<.001	…	…	…
BLBLI	34[d] (47.2)	0	<.001	…	…	…
Empirical therapy						
Carbapenem	…	…	…	0	30 (25)	<.001
BLBLI	…	…	…	45[d] (83.3)	38 (31.7)	<.001
Cephalosporins	…	…	…	7 (13)	39 (32.5)	.006
Fluoroquinolones	…	…	…	2 (3.7)	13 (10.8)	.1[c]
Appropriate empirical therapy	…	…	…	34 (63)	64 (53.3)	.2
Mortality, no. of deaths						
Day 7	2 (2.8)	3 (9.7)	.1[c]	1 (1.9)	5 (4.2)	.6[c]
Day 14	7 (9.7)	5 (16.1)	.3	3 (5.6)	14 (11.7)	.2
Day 30	7 (9.7)	6 (19.4)	.1	5 (9.3)	20 (16.7)	.1
Hospital stay after BSI , median (IQR), d	12 (8–28)	13 (9–25)	.7[b]	13 (8–22)	13 (10–25)	.04[b]

β-lactam/β-lactamase inhibitors

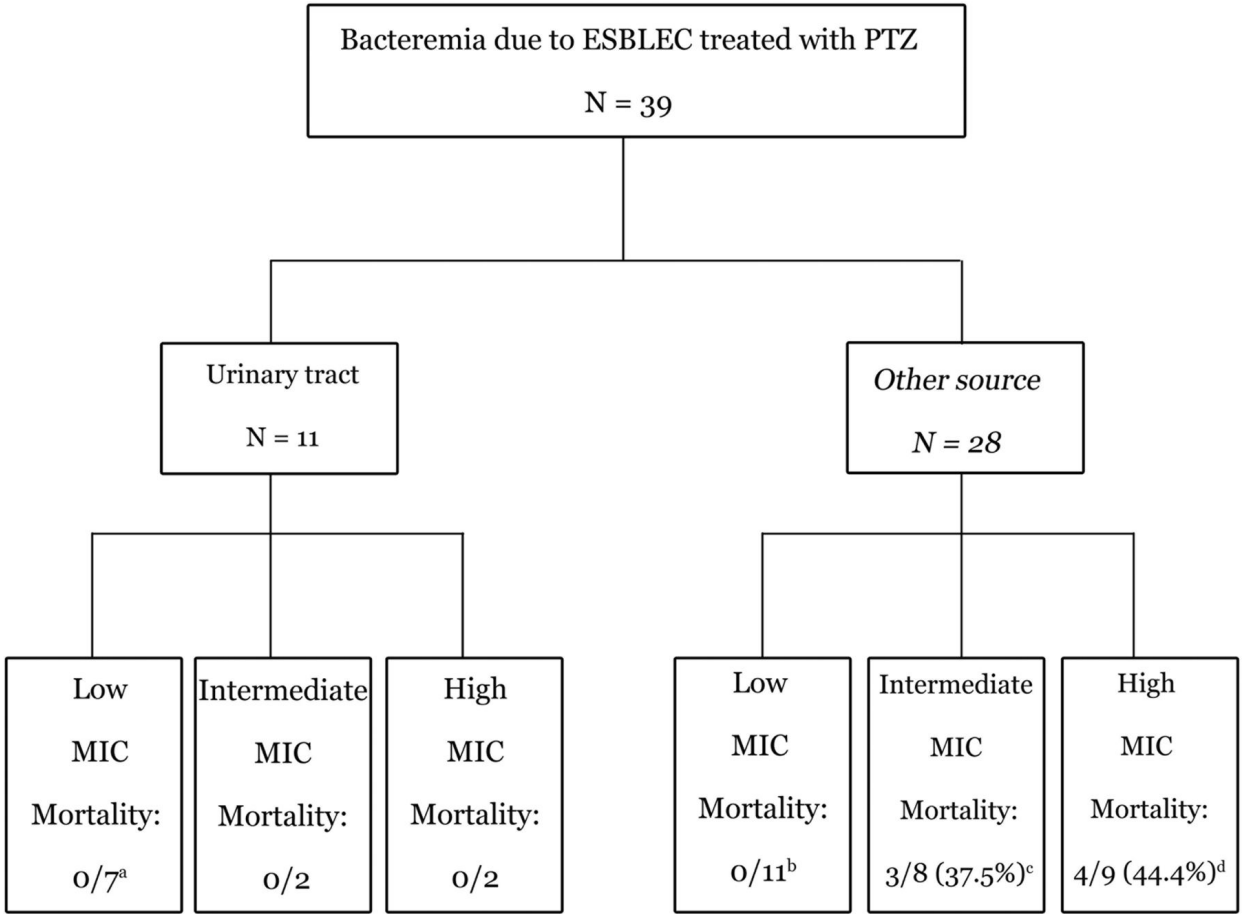
Therapy	Mortality rate at 30 days	
	Empiric (BLBLI: 72)/ Carbapenem: 31)	Definitive (BLBLI: 54/ Carbapenem: 120)
BLBLI	9.7%	9.3%
Carbapenem	19.4%	16.7%

Table 3. Mortality at 30 Days in Patients Who Received Empirical Therapy With an Active β-Lactam/β-Lactam Inhibitor, According to Minimum Inhibitory Concentration of the Antimicrobial Used[a]

	Minimum Inhibitory Concentration, mg/L				
Antimicrobial	≤1	2	4	8	16
Piperacillin-tazobactam	0/10	0/8	1/4	2/6	1/7
Amoxicillin-clavulanate	…	…	1/12	2/25	…

[a] Data are expressed as No. of patients who died/No. of patients treated.

Piperacillin-tazobactam and ESBL E.coli



Piperacillin-tazobactam for ESBL bacteremia

- Retrospective cohort study, single center, 7 years
- N=214: 103 in PTZ empirically, 110 in Carbapenem
  - *Escherichia coli*, *Klebsiella* spp, *Proteus marcescens*

	Complete Cohort (N = 213)		
Characteristic	PTZ/Carbapenem (n = 103 [48%])	Carbapenem (n = 110 [52%])	*P* Value
Age, mean (SD)	48.1 (22.8)	48.2 (19.0)	.96
Male sex, No. (%)	59 (57.3)	72 (60.5)	.63
Pitt bacteremia score, mean (SD)	2.3 (1.9)	2.1 (1.3)	.15
ICU-level care, day 1	33 (32.0)	39 (35.5)	.70
ANC ≤100 cells/μL, No. (%)	16 (15.5)	16 (13.4)	.66
Likely source of bacteremia, No. (%)			
Central line associated	45 (43.7)	52 (43.7)	1.00
Urinary tract	20 (19.4)	24 (20.2)	.89
Biliary	7 (6.8)	12 (10.1)	.38
Intra-abdominal	20 (19.4)	16 (13.4)	.23
Pneumonia	11 (10.7)	9 (7.6)	.43

Piperacillin-tazobactam for ESBL bacteremia

- 14 day mortality:
  - 17 deaths in the PTZ grp vs. 9 deaths in the Carbapenem grp

Table 2. Fourteen-Day Mortality for 213 Patients With Extended-Spectrum β-Lactamase Bacteremia Treated Empirically With Piperacillin-Tazobactam or Carbapenem Therapy in a Stabilized Inverse Probability–Weighted Cohort[a]

	Univariable Analysis			Multivariable Analysis		
Characteristic	HR	95% CI	*P* Value	Adjusted HR[a]	95% CI	*P* Value
Piperacillin-tazobactam	1.78	1.00–3.13	.05	1.92	1.07–3.45	.03
Age (per 10-y increase)	1.28	1.09–1.50	.11	1.18	0.99–1.41	.07
Pitt bacteremia score	1.55	1.39–1.72	<.001	1.49	1.28–1.72	<.001
Intensive care unit level care, day 1	4.49	2.53–7.98	<.001	4.25	1.86–9.71	<.001
Immunocompromised	1.09	0.62–1.93	.76	. . .	. . .	. . .
Inadequate source control[b]	1.18	0.81–1.72	.39	. . .	. . .	. . .

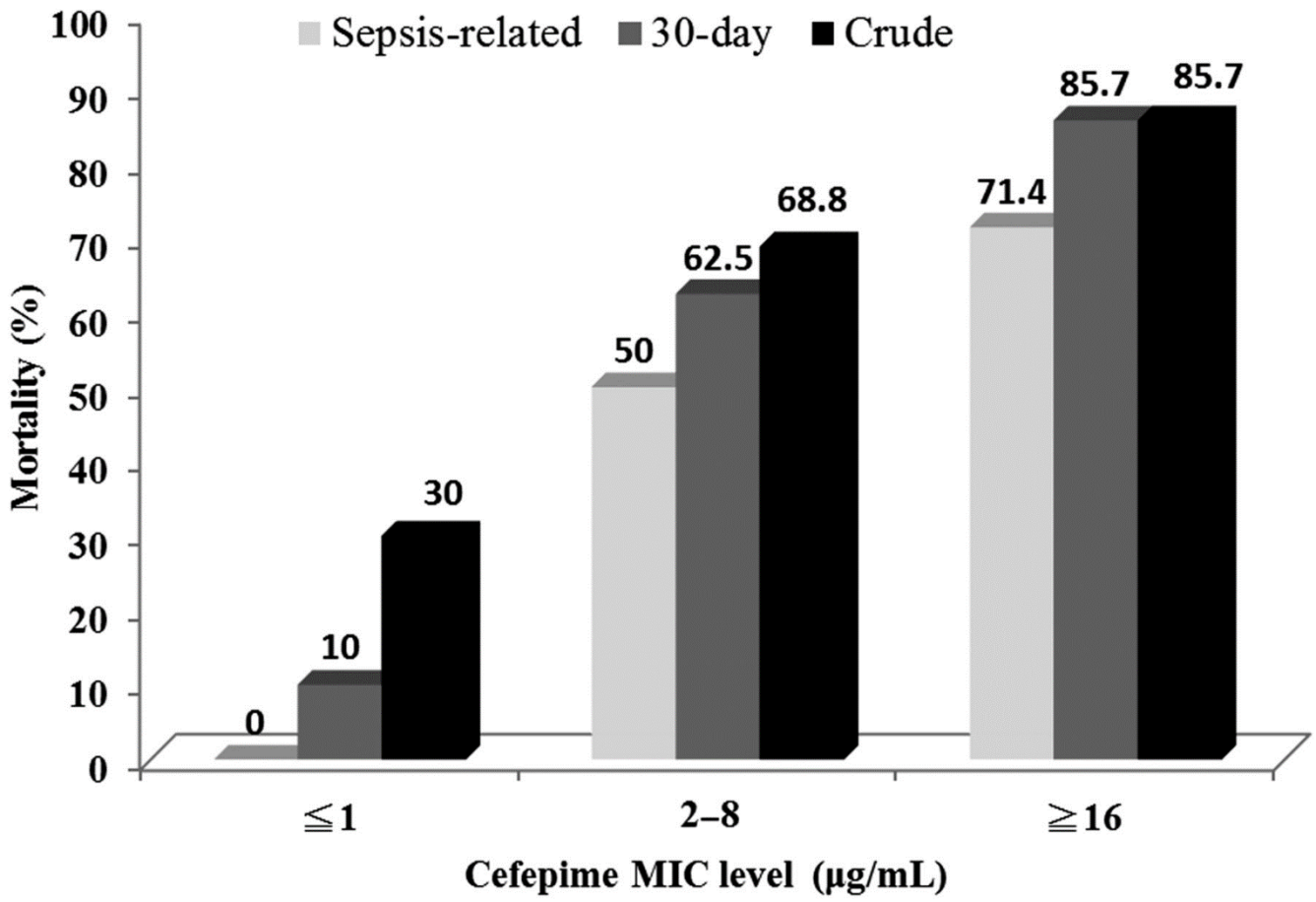
- Differences between 2 studies:
  - Source of infection
  - ESBL E.coli vs Other ESBL producers
  - Dosing strategy

Cefepime therapy for ESBL bacteremia

Retrospective study of ESBL bacteremia

- 178 patients in definitive therapy cohort
- Cefepime (in-vitro activity confirmed) (n=17) versus carbapenem (n=161)
  - Cefepime patients:
  - ↑ clinical failure (OR, 6.2; 95% CI 1.7-22.5; p=0.002)
  - ↑ microbiological failure (OR, 5.5; 95% CI 1.3-25.6; p=0.04)
  - ↑ 30 day mortality (OR, 7.1; 95% CI 2.5-20.3; p<0.001)
  - No difference in hospital length of stay
- Multivariate analysis: definitive cefepime therapy, Pitt bacteremia score ≥4 points, and rapidly fatal disease associated with 30-day mortality

Cefepime therapy for ESBL bacteremia



CHI Memorial / Lee NY, et al. Clin Infect Dis 2013;56:488-95

Summary

ESBL producing organisms

- Cefepime may not be a safe option for severe ESBL bloodstream infections
  - Worse outcomes seen as MICs for cefepime increases

- Piperacillin-tazobactam is a reasonable option in patients with a urinary or biliary source (mild)
  - Optimize doses

- Initiate carbapenem therapy in severely ill patients with a high suspicion for ESBL infection