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<th>Study / Location</th>
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| Sharara¹ (2019)  | Multicenter, retrospective, observational, propensity-score weighted cohort | N=188 (full cohort), N=186 (propensity-score weighted cohort) | Inclusion criteria  
- Urine Cx growing *E. coli*, *K. pneumoniae*, *K. oxytoca*, or *P. mirabilis*  
- Presence of an ESBL gene | Propensity-score weighted cohort: N=186  
- PZT (n=45)  
- Carbapenem (n=141) | Persistence of an ESBL gene  
- 30-day recurrent cystitis or pyelonephritis with same organism (P=0.52)  
- PZT (20%)  
- Carbapenem (24.8%) | Monomicrobial UTI  
(either ESBL *E. coli*, *K. pneumoniae*, *K. oxytoca*, or *P. mirabilis*)  
Extended-infusion dosing not mentioned  
Post-discharge data may have been missing  
Resistance patterns undisclosed but may have varied across sites  
Identification of carbapenem-resistant spp in 60 days (P<0.09) |
| Naris² (2019)    | Retrospective, single center cohort | N=295 | Inclusion criteria  
- Adults ≥18 yr  
- Sepsis 2/2 ESBL and CTX-R *E. coli* BSI | Empiric treatment regimens  
- BLBLI  
- Carbapenem | Multivariable logistic regression for risk factors impacting mortality  
- Pitt bacteremia score ≥4 (OR=16.85, 95%CI 7.47-38.00, P<0.001)  
- Urinary source (OR=0.33, 95%CI 0.15-0.73, P=0.06) | Monomicrobial (CTX-R *E. coli*)  
Dosing regimens not specified  
Specific BLBLI and carbapenem ABx not specified  
No significant effect on mortality from use of either BLBLI or carbapenem for either empiric or definitive treatment |
| Benanti³ (2019)  | Retrospective, single center cohort | N=103 | Inclusion criteria  
- Adults with leukemia or Hx of hematopoietic stem cell transplant (HCT)  
- ESBL *E. coli* BSI  
- Empiric treatment with either PZT, carbapenem, or CPM | Empiric treatment regimens  
- PZT (n=21)  
- 4.5 g IV q6h  
- Carbapenem (MERO, n=42)  
- 1 g IV q8h  
- CPM (n=40)  
- 2 g IV q8h | Multivariable analysis showed higher Pitt bacteremia scores significantly associated with increased mortality (HR 2.21, 95%CI 1.56-3.13, P=0.01) | Monomicrobial (ESBL *E. coli*)  
Most common BSI source: intra-abdominal  
Intermittent/standard infusion dosing (30-minute infusion)  
Persistent BSI 36% with PZT vs 5% with carbapenem (P=0.03) |
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<th>Empiric Treatment Regimens</th>
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<th>Definitive Outcome</th>
<th>Subgroup Analyses</th>
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<tr>
<td>John (2019)</td>
<td>Multicenter, retrospective chart review</td>
<td>U.S.A.</td>
<td>117</td>
<td>Adults with ESBL BSI who received empiric treatment with at least 1 dose of either PZT or a carbapenem prior to positive Cx</td>
<td>Pregnant or incarcerated patients</td>
<td>PZT (n=66) Carbapenem (n=51)</td>
<td>PZT: 3% Carbapenem: 7.8%</td>
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<td>Harris (2018)</td>
<td>Prospective, open-label, parallel group, multicenter, non-inferiority RCT</td>
<td>International</td>
<td>379</td>
<td>Adult inpatients with ≥1 blood Cx (+) for E. coli or Klebsiella spp. (CTX-R, PZT-S, MERO-S) who received definitive therapy with either treatment regimen</td>
<td>Allergy to trial drugs or similar ABx classes Survival expectancy &lt;96 hr Polymicrobial BSI Requirement for concomitant ABx with activity against GNRs</td>
<td>PZT (n=188) Carbapenem (n=191)</td>
<td>PZT: 23/187 = 12.3% MERO: 7/191 = 3.7%</td>
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<td>Tullos (2018)</td>
<td>Retrospective, multicenter cohort</td>
<td>U.S.A.</td>
<td>180</td>
<td>Age ≥ 18 years Positive urine Cx with an ESBL-producing organism Received ≥48 hr of definitive treatment with PZT or carbapenem</td>
<td>Concomitant BSI Isolates resistant to treatment regimen</td>
<td>PZT (n=39) Carbapenem (n=141)</td>
<td>PZT: 74.4% Carbapenem: 80.9%</td>
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<td>Study</td>
<td>Design</td>
<td>Inclusion criteria</td>
<td>Exclusion criteria</td>
<td>Treatment</td>
<td>Treatment failure</td>
<td>Multivariate analyses for predictors of treatment failure</td>
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| Yoon (2017) | Retrospective, single center, observational | N=150  
- Adults with acute pyelonephritis 2/2 ESBL E. coli  
  o Stratified as community-onset (within 48 hr of hospital admission) or nosocomial (after 48 hr of hospital admission) |  
- Polymicrobial infections  
- Recurrent pyelonephritis cases  
- Structural GU abnormalities (not including foley catheter) | Initial effective therapy, continued for at least 3 days (doses renally adjusted)  
- PZT (n=68)  
  o 4.5 g IV q8h  
- ERTA (n=82)  
  o 1 g IV q24h | Composite of in-hospital mortality, change in initial ABx, and microbiological cure failure |  
- Septic shock (OR 4.27; 95%CI 1.66-10.99)  
- Recent immunosuppression treatment (OR 2.84; 95%CI 1.02-7.91) |
| Ko (2017) | Multicenter, retrospective, propensity score-weighted cohort | N=232  
- Adults ≥18 yr with ESBL E. coli or K. pneumoniae BSI  
- Empiric therapy with either carbapenem or non-carbapenem  
- Definitive therapy with carbapenem |  
- Repeat BSI episodes  
- Empiric ABx <48 hrs  
- Combination ABx treatment  
- Treatment with inappropriate definitive ABx  
- Polymicrobial infections  
- Patients out of standard care | Empiric therapy  
- Non-carbapenem (n=49)  
  o PZT (n=41)  
  o FQs (n=8)  
- Carbapenem (n=183) | 30-day all-cause mortality (P=0.42)  
- Non-carbapenem: 6.3%  
- Carbapenem: 11.4% |  
- Multicenter  
- Monomicrobial (ESBL E. coli)  
- Pyelonephritis Dx included presence of symptoms, positive U/A (including pyuria), and positive urine Cx  
- Blood isolates were 72.6% susceptible to PZT, 33.6% to CIPRO, and 98.5% to MERO |
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<tr>
<th>Study</th>
<th>Design, Location</th>
<th>N</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
<th>Doses (adjusted for renal impairment), treatment duration 10-14 days</th>
<th>Clinical Success (P&lt;0.001)</th>
<th>Microbiological Success (P&lt;0.001)</th>
<th>30-day Mortality</th>
<th>Other Findings</th>
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<tbody>
<tr>
<td>Seo et al. (2017)</td>
<td>South Korea, Multicenter, RCT</td>
<td>72</td>
<td>Hospitalized adult patients with fever, HA-UTI 2/2 ESBL E. coli</td>
<td>Any co-infection(s), ABx use in previous 7 days, Complicating urinary factors that could not be effectively treated during the trial</td>
<td>PZT (n=33)</td>
<td>PZT: 93.9%</td>
<td>PZT: 97%</td>
<td>30.9% vs carbapenem 29.8% (P=0.89)</td>
<td>Monomicrobial (ESBL E. coli)</td>
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<td>CPM (n=6)</td>
<td>CPM: 33.3%</td>
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<td>Multivariable analysis showed empiric carbapenem use as only significant risk factor for MDR infections</td>
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<tr>
<td>Ng et al. (2016)</td>
<td>Singapore, Retrospective, multicenter cohort</td>
<td>151</td>
<td>Monomicrobial BSI receiving active empiric therapy with either PZT or carbapenem ≥48 hr</td>
<td>Polymicrobial BSI, Empiric therapy for &lt;48 hr, Repeat BSI episodes</td>
<td>PZT (n=94)</td>
<td>Unadjusted: PZT 30.9% vs carbapenem 29.8% (P=0.89)</td>
<td></td>
<td>Cefepime recruitment stopped due to treatment failure</td>
<td>Monomicrobial (ESBL E. coli or K. pneumoniae) Most common BSI source: UTI Dosing protocol allowed for extended infusion PZT (3 hours) but not carbapenems Patients receiving carbapenems less likely to have healthcare-associated risk factors (38.6% vs 59.6% for PZT) 30-day MDR and fungal infection rates (PZT 7.4% vs MERO 24.6%, P&lt;0.01) Multivariable analysis showed empiric carbapenem use as only significant risk factor for MDR infections</td>
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<tr>
<td>Country</td>
<td>Study Type</td>
<td>Inclusion Criteria</td>
<td>Doses (adjusted for renal impairment)</td>
<td>14-day mortality (P=0.03)</td>
<td>30-day mortality (P=0.065)</td>
<td>30-day all-cause mortality (P=0.02)</td>
<td>Monomicrobial (either ESBL E. coli, K. pneumoniae, K. oxytoca, or P. mirabilis)</td>
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| Spain        | Retrospective, single center cohort | N=213  
Inclusion criteria  
• Any monomicrobial ESBL BSI that received PZT or carbapenem | PZT (n=103)  
• Carbapenems (n=110)  
  o MERO 1 g IV q8h  
  o IMI/C 500 mg IV q6h  
  o ERTA 1 g IV q24h | HR 1.92 (95%CI 1.07-4.5) for empiric PZT vs carbapenems | 14.3% carbapenem vs 23.1% PZT | 19.1% carbapenem vs 30.8% PZT | Most common ESBL BSI infection: CLABSI  
Duration of infusions not reported  
Higher Pitt bacteremia scores and ICU admission also significantly associated with increased 14-day mortality risk |
| Taiwan       | Retrospective, multicenter cohort | N=40  
Inclusion criteria  
• Age ≥18 yr  
• ESBL P. mirabilis BSI  
• Received at least 48 hr of therapy | PZT 4.5 g IV q6h (n=13)  
• Carbapenems (n=21)  
  o ERTA 1 g IV q24h  
  o IMI/C 500 mg IV q6h  
  o MERO 1 g IV q8h  
• Other agents (n=6) | 0% low MIC vs 41.4% other MICs | 0% low MIC vs 15.4% other MICs | In-hospital mortality (P=0.68) | Most common BSI coinfection: urosepsis  
Duration of infusions not reported |
| Spain        | Merged database analysis of 6 prospective cohorts | N=39  
Inclusion criteria  
• Age ≥17 yr  
• ESBL E. coli BSI treated with empiric PZT  
• Stratification by isolate’s PZT MIC  
  High MIC: MIC ≥16 mg/L (28.2%)  
  Intermediate MIC: MIC 4-8 mg/L (25.6%)  
• Low MIC: ≤2 mg/L (46.1%)  
• First empiric PZT dose given within 24 hr of obtaining blood Cx  
• PZT 4.5 g IV q6h | 0% low MIC vs 41.4% other MICs | 0% low MIC vs 15.4% other MICs | In-hospital mortality (P=0.68) | Most common BSI coinfection: urosepsis  
Duration of infusions not reported |
| Spain        | Post-hoc analysis of 6 prospective cohorts | N=192  
Inclusion criteria  
• Age >17 yr  
• Clinically significant sepsis  
• ESBL E. coli BSI  
• Empiric therapy with BLBLI or carbapenem for >48 hours  
• Created 2 non-mutually exclusive cohorts  
  • Empiric therapy cohort (ETC), n=103  
    o Empiric monotherapy within 24 hr of drawing blood Cx  
    o Definitive therapy cohort (DTC), n=174  
    o Definitive monotherapy for ≥50% of total Abx duration | BLBLI  
  o PZT 4.5 g IV q6h  
  o AMOX/CLAV 1.2 g IV q8h  
  o Carbapenem  
    o IMI/C 500 mg IV q6h  
    o MERO 1 g IV q8h  
    o ERTA 1 g IV q24h | 0% low MIC vs 41.4% other MICs | 0% low MIC vs 15.4% other MICs | In-hospital mortality (P=0.68) | Most common BSI coinfection: urosepsis  
Duration of infusions not reported |

**Abbreviations:** 2/2 = secondary to; 95%CI = 95% confidence interval; Abx = antibiotic; AMOX/CLAV = amoxicillin-clavulananate; BLBLI = beta lactam/beta-lactamase inhibitor; BSI = bloodstream infection; CIPRO = ciprofloxacin; CLABSI = central line-associated bloodstream infection; CPM = cefepime; CTX-R = ceftaxime-resistant; Cx = culture; Dx = diagnosis; ERTA = ertapenem; ESBL = extended-spectrum beta-lactamase inhibitor; FQ = fluoroquinolone; GNR = Gram-negative rod; GU = genitourinary; HA-UTI = healthcare-associated urinary tract infection; HR = hazard ratio; Hx = history; ICU = intensive care unit; IMI/C = imipenem/clastatin; IV = intravenous; LOS = length of stay; MERO = meropenem; MERO-S = meropenem-sensitive; MIC = minimum inhibitory concentration; MDR = multidrug resistant; OR = odds ratio; pt = patient; PZT = piperacillin/tazobactam; PZT-S = piperacillin/tazobactam-sensitive; RCT = randomized controlled trial; spp = species; STROBE = Strengthening the Reporting of Observational Studies in Epidemiology; UTI = urinary tract infection.