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Background. Opioid addiction in the United States has reached epidemic proportions threatening public health. This analysis evaluates the baseline characteristics and bacterial causes of ABSSSI in patients who were IVDU from two parallel Phase 3 trials comparing the treatment of iclaprim with vancomycin.

Methods. A total of 621 patients who were IVDU from two parallel Phase 3, double-blind, randomized (1:1), active-controlled, multinational, multicenter trials (REVIVE-1 and REVIVE-2) were analyzed both separately and pooled. This post-hoc analysis summarizes the baseline bacterial causes of ABSSSI identified among IVDU. Per protocol, ABSSSI (major abscesses, cellulitis, or wound infections) were defined as having either the presence of purulent or seropurulent drainage before or after surgical intervention of the wound or at least 3 of the following signs and symptoms: discharge, erythema (extending at least 2 cm beyond the wound edge in any direction), swelling and/or induration, heat and/or localized warmth, and/or pain and/or tenderness to palpation. IVDU was defined based on subjected-reported medical history. At the baseline visit, ABSSSI were sampled for microbiological culture. Cultures were performed locally, and isolates were submitted to the central microbiology laboratory.

Results. Among IVDU with ABSSSI, average age was 44 years, 67.6% were male, average lesion size was 322 cm^2, 10.8% had abnormal renal function (CrCl ≤ 90 mL/minute), and 3.9% had bacteremia. The bacterial causes of ABSSSI among IVDU are shown in the Table.

Conclusion. IVDU, a growing population, are vulnerable to ABSSSI. *S. aureus*, including MRSA, and *S. anginosus* group were the most commonly identified bacterial causes of ABSSSI in patients who are IVDU. Therefore, antibiotic selection should cover these bacteria among IVDU who present with an ABSSSI.

	Baseline Microbiology, n (%) (n=621)
*S. aureus**	371 (59.7%)
MRSA	194 (31.2%)
MSSA	188 (28.7%)
S. pyogenes	32 (5.2%)
Streptococcus agalactiae	1 (0.2%)
Streptococcus anginosus group	107 (17.2%)

*Percentages do not add to 100% because some patients had more than one baseline pathogen identified from their ABSSSI.

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2290. Carbapenem vs. Piperacillin–tazobactam Definitive Therapy for Patients with Bloodstream Infections Due to Ceftriaxone Not Susceptible *Escherichia coli* or *Klebsiella* species

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Background. Definitive therapy with piperacillin–tazobactam (TZP) for ceftriaxone (CRO)-resistant *E. coli* or *K. pneumoniae* bloodstream infections (BSI) has been shown to be inferior to carbapenem therapy in a randomized trial.

Methods. The Premier US database was queried for hospitalized patients with monomicrobial *E. coli* or *Klebsiella* spp BSI that were not susceptible (NS) to CRO between June 2015 and May 2018. Adults with index positive blood culture(s) drawn within the first 2 hospital days who were treated with active antibiotic therapy that continued for ≥3 consecutive days were included. We defined antibiotics administered on or prior to Day 3 as empirical therapy and all subsequent days as definitive therapy. Outcomes among patients who received definitive therapy with a carbapenem vs. TZP were evaluated.

Results. There were 954 patients (mean age, 67.6 years; 52.4% women) who met selection criteria and received active empirical therapy. 729/954 received carbapenem definitive therapy and 38/954 received TZP definitive therapy. Median Charlson Comorbidity Index scores were similar between carbapenem and TZP definitive therapy groups (6 vs. 5, $P = 0.78$). Crude 14-day in-hospital mortality for CRO-NS BSI due to *E. coli* or *Klebsiella* spp. was 4.4%. Definitive therapy with TZP (6/38; 15.8%) was associated with an increased likelihood of 14-day mortality relative to that of a carbapenem (22/729; 3.0%; $P < 0.0001$). The increased 14-day mortality observation was consistent in a multivariate cox proportional hazards model (adjusted hazard ratio, 5.70; 95% CI, 2.09 to 13.23; $P = 0.002$). Of patients who received carbapenem definitive therapy, 14-day mortality was 2.7% (19/693) if a carbapenem was part of empirical therapy and 8.3% (3/36; $P = 0.06$) if empirical therapy did not include a carbapenem. Median post-blood culture length of stay (7 vs. 6 days, $P = 0.65$) and hospital costs ($13,886 vs. $13,559, $P = 0.62$) were similar between carbapenem and TZP definitive therapy groups</./p>

Conclusion. In this large US database, definitive therapy with TZP was associated with an increased likelihood of 14-day mortality relative to that of definitive carbapenem therapy in patients with CRO-NS BSI due to *E. coli* or *Klebsiella* spp. These findings support recent clinical evidence in favor of definitive carbapenem therapy for CRO-NS BSI due to *E. coli* or *Klebsiella* spp.

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2291. Evaluation of Multidrug-Resistant *Pseudomonas aeruginosa* Isolates in Patients Receiving Ceftolozane/tazobactam

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Background. Multidrug-resistant (MDR) *Pseudomonas aeruginosa* is a challenging pathogen to treat. Ceftolozane/tazobactam (C/T) is a combination cephalosporin and β-lactamase inhibitor that has demonstrated activity against MDR *P. aeruginosa*, including carbapenem-resistant isolates. The objective of this study was to evaluate multidrug resistance in *P. aeruginosa* isolates obtained from patients treated with C/T across the Veterans Affairs (VA) Healthcare System nationally.

Methods. Hospitalized patients who received at least 1 dose of CT between January 2015 and April 2018 and had a positive *P. aeruginosa* culture were included in this retrospective study. Culture source and antimicrobial susceptibility reports were assessed for each *P. aeruginosa* isolate. Isolates were categorized as multidrug-resistant based on the Centers for Disease Control (CDC) definition. Resistance rates were categorized by source of culture.

Results. We identified 174 positive *P. aeruginosa* cultures among 154 patients who received at least one dose of C/T during the study period. The most common sources of isolates were lung (40% of patients), urine (21%), skin and soft tissue (15%), blood (14%), and bone/joint (14%). Most patients (98.1%) had isolates that were MDR, with high rates of carbapenem (84.4%), extended-spectrum cephalosporin (82.5%), and fluoroquinolone (79.9%) resistance. In this cohort, 50.6% of patients received at least one antibiotic prior to initiating C/T to which their clinical culture was not susceptible.

Conclusion. Antibiotic resistance was high in this cohort of patients with *P. aeruginosa*, and as a result, use of non-susceptible antibiotics occurred in 50.6% of patients before C/T was started. The high carbapenem resistance rates are of great clinical concern, but highlight an area of utilization for C/T given its activity against carbapenem-resistant *P. aeruginosa*.

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2292. Incidence of Acute Kidney Injury Associated with Duration of Vancomycin and Piperacillin/tazobactam Combination Therapy

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Background. Empiric antibiotic therapy for serious and healthcare-acquired infections often requires coverage for resistant pathogens, including methicillin-resistant Staphylococcus aureus (MRSA) and Pseudomonas aeruginosa. These regimens commonly consist of vancomycin plus an antipseudomonal β-lactam. Recent studies have reported increased acute kidney injury (AKI) risk associated with concomitant vancomycin and piperacillin/tazobactam therapy compared with each agent alone. The objective of this study was to determine whether vancomycin with piperacillin/tazobactam had an increased AKI incidence compared with vancomycin plus cefepime or meropenem. Furthermore, data were analyzed to determine whether a specific duration was associated with an increased AKI incidence.

Methods. A retrospective cohort study was conducted analyzing patients who received vancomycin in combination with piperacillin/tazobactam (V+PT), cefepime (V+C), or meropenem (V+M) between January 1, 2018 through June 30, 2018. Adult patients with normal baseline renal function and receipt of at least 48 hours of combination therapy, with the two antibiotics initiated within 24 hours of one another, were included. AKI events, evaluated using the Acute Kidney Injury Network (AKIN) criteria, during antibiotic therapy and up to 72 hours after antibiotic discontinuation were recorded. This data were used to calculate the AKI incidence with each regimen and AKI incidence associated with each day of therapy.

Results. A total of 181 patients were included in the study. The incidence of AKI in the V+PT group was 22.8% vs. 5.6% and 16.7% in the V+C and V+M groups, respectively ($P = 0.237$). Median duration of therapy when AKI occurred was 3 days for V+PT, 4 days for V+C, and 2 days for V+M ($P = 0.015$). Patients in the V+M group received more nephrotoxic agents compared with V+PT and V+C ($P = 0.004$). Statistical analysis did not find a specific day of V+PT therapy predictive of AKI. However, a time to event analysis demonstrated a steady increase in AKI risk with V+PT from day 2 through 6.

Conclusion. Although not statistically significant, V+PT therapy was associated with a higher incidence of AKI compared with V+C or V+M. Future studies are needed to further assess the impact of duration of therapy on AKI incidence.

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